DEPARTMENTS OF LABOR, HEALTH AND HUMAN SERVICES, EDUCATION, AND RELATED AGENCIES APPROPRIATIONS FOR 1987

HEARINGS

BEFORE A

SUBCOMMITTEE OF THE

COMMITTEE ON APPROPRIATIONS

HOUSE OF REPRESENTATIVES

NINETY-NINTH CONGRESS

SECOND SESSION

SUBCOMMITTEE ON THE DEPARTMENTS OF LABOR, HEALTH AND HUMAN SERVICES, EDUCATION, AND RELATED AGENCIES

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NATIONAL INSTITUTES OF HEALTH

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DEPARTMENTS OF LABOR, HEALTH AND HUMAN SERVICES, AND EDUCATION, AND RELATED AGENCIES APPROPRIATIONS FOR 1987

FRIDAY, MARCH 14, 1986.

NATIONAL INSTITUTES OF HEALTH

NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

WITNESSES

DR. DUANE ALEXANDER, DIRECTOR

DR. WILLIAM F. RAUB, DEPUTY DIRECTOR FOR EXTRAMURAL RESEARCH AND TRAINING, NIH

DR. HEINZ W. BERENDES, DIRECTOR, EPIDEMIOLOGY AND BIOMETRY RESEARCH PROGRAM

DR. FLORENCE P. HASELTINE, DIRECTOR, CENTER FOR POPULATION RESEARCH

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ARTHUR D. FRIED, BUDGET OFFICER

DENNIS P. WILLIAMS, ACTING DEPUTY ASSISTANT SECRETARY, BUDGET, DEPARTMENT OF HEALTH AND HUMAN SERVICES

Mr. NATCHER. At this time, we take up the budget request for the National Institute of Child Health and Human Development.

We have before the committee Dr. Alexander, the Director. It is a pleasure to have you back before the committee.

Before you give us your statement, tell us who you have with you at the table there.

Dr. ALEXANDER. It is a pleasure to be back. Beginning on my left, accompanying me are Dr. Berendes, Director of our Epidemiology and Biometry Research Program; Mr. Fried, Budget Officer; Mr. Hedetniemi, the Executive Officer; Dr. Raub, NIH Deputy Director for Extramural Research and Training, sitting in for Dr. Wyngaarden; Dr. Haseltine, the Director of our Center for Population Research; and Mr. Williams from the Department.

Mr. NATCHER. We are delighted to have all of you ladies and gentlemen, and we will be pleased to hear from you.

Dr. ALEXANDER. Thank you, Mr. Chairman. Anniversaries occurring in 1987 have been mentioned several times in these hearings. Next year, 1987, the NICHD also will have an important anniversary. It will make the 25th year since the NICHD was established by the Congress to address some of the most important public health problems facing our Nation.

The statement I submitted for the record outlines some of our progress and plans regarding these problems. I want now to highlight just a few.

LOW BIRTH WEIGHT PREVENTION

Foremost among these is improving pregnancy outcome and reducing infant mortality. Here, the primary target of our efforts is to prevent low birth weight. Two-thirds of all infants who die are low birth weight, that is born weighing less than five and one-half pounds.

Through research, we now save half of the babies born weighing 2 pounds, but the costs and complications associated with low birth weight mean we must focus primarily on prevention.

To this end, the NICHD two years ago developed a low birth weight prevention initiative to which we have devoted increasing resources. Two new centers focusing on intrauterine growth retardation research have recently been funded. The networks of maternal-fetal medicine units and neonatal intensive care units we are establishing as part of this initiative become operational this month. They will provide a system for clinical trials to test quickly new obstetric and neonatal techniques to prevent low birth weight or to improve outcome of premature infants.

Because maternal behavior is such an important factor in low birth weight, our scientists have helped design and fund an intervention study in the District of Columbia intended to identify high-risk women early in pregnancy, encourage them to enter early regular prenatal care, and eliminate behaviors such as smoking and alcohol consumption that increase the likelihood of low birth weight and infant mortality or morbidity.

BIRTH DEFECTS

Birth defects are the leading overall cause of infant mortality. Our scientists have identified some of the genes involved in earliest embryonic development, and are studying in animal models how they turn on or off or misfunction to cause malformations.

SUDDEN INFANT DEATH SYNDROME

Sudden Infant Death Syndrome is the leading cause of infant mortality from one month to one year. We have demonstrated that SIDS is not related to DPT immunization, as some have claimed, and we are encouraging scientists to pursue new leads on this mysterious condition.

CHILDHOOD INJURIES

Injuries are the leading killer and disabler of children from age one to adulthood. Our behavioral scientists have developed effective ways to reduce auto injury and scalding among children, and are extending this work to other areas of injury prevention.

MENTAL RETARDATION

Mental retardation is the major reason for children not achieving their potential, but we are steadily adding to the number of causes of mental retardation that are eliminated. The major cause of acquired mental retardation in this country is now meningitis due to *H. influenzae* infection, which results in 3,000 to 5,000 cases of mental retardation per year.

VACCINE DEVELOPMENT

Our intramural scientists have developed a vaccine that we expect will be protective against this disease in infancy, and we will launch a field trial of it along with our new pertussis vaccine this year.

Let me elaborate for a minute, if I may, Mr. Chairman, on these vaccines, because their potential impact is so enormous.

An *H. influenzae* vaccine developed by our scientists was recently licensed for use in children over age 2. It is a pure chemical and has already been given to more than 4 million children without a single side-effect reported. The modified vaccine our scientists have devised for use in infancy is now in early human trials and looks equally promising and effective.

The improved pertussis vaccine we have developed in our laboratories is a toxoid vaccine. Our scientists have demonstrated that pertussis or whooping cough is caused by a chemical toxin produced by the pertussis bacteria, and that immunity only to the toxin creates total protection against the disease.

By growing the bacteria, extracting the toxin, and inactivating the toxin to produce a harmless toxoid, we have produced a vaccine that is far more effective than the present vaccine and should be totally free of side-effects.

We will begin initial human studies of this pertussis vaccine in adults next month in the NIH Clinical Center and will initiate a large field trial in Sweden this summer. We also are planning a major trial in the United States involving the entire State of Massachusetts.

I also mentioned in my statement a typhoid vaccine we have developed. This vaccine, like the *H. influenzae* vaccine, is a pure chemical and costs 10 cents per dose to produce.

Our scientists returned this week from Nepal, where in two weeks they completed its initial field trial, immunizing 6500 persons with this vaccine with no adverse reactions. Because typhoid fever is so common there, we will have evidence of its effectiveness within one year.

These three vaccines have a common feature. The diseases they will prevent, whooping cough, typhoid fever, and *H. influenzae* infection, have no known animal reservoir; they infect only humans.

In this way, they are like smallpox, and so, as with smallpox, broad use of these vaccines has the potential to totally eliminate these diseases from the planet, so that eventually even immunization against them would be unnecessary.

This is really the ultimate in prevention. We not only eliminate the disease, but we eliminate the need for the prevention measure as well.

POPULATION RESEARCH

Let me turn now to our population research program. Half of all pregnancies in this country are still unintended. One of our grantees, Nobel Prize Laureate Dr. Roger Guillemin, a few months ago isolated and determined the structure of inhibin, a protein that we think will be a new type of contraceptive.

This long-sought substance specifically inhibits sperm formation and ovulation without affecting other sexual functions, and we will pursue work on inhibin as part of our contraceptive development initiative.

TEENAGE PREGNANCY

Teenage pregnancy has received increasing public attention recently, and it should because of its enormous ramifications for our society, both short-term and long-term.

The NICHD has had a long-standing research program in teenage pregnancy, and many of the data cited regarding this problem come from our research. We are increasing this effort, and later this year NICHD will be funding several studies focusing on teen sexual behavior and contraception. These studies will provide valuable information to guide programs seeking to reduce teenage pregnancy.

FY 1987 BUDGET REQUEST

The work of this Institute helps to assure the birth of healthy children and wanted children, and to provide an opportunity for all children to achieve their full potential. Our request for fiscal year 1987 is $309,119,000.

I will be pleased to answer your questions.

[The statement of Dr. Alexander follows:]

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Statement of the Director National Institute of
Child Health and Human Development

There are many complex biological and behavioral processes involved in the successful achievement of each major step in the life cycle--reproduction, pregnancy, birth, and development from infancy and childhood to adulthood. There are also many opportunities for problems to arise. Because each step is so fundamental to the development of a healthy, functional adult, difficulties during any of them can result in some of the most devastating and costly human problems: infant mortality, birth defects, injuries, learning disorders, mental retardation, infertility, and unintended pregnancies.

Herein lies the difficult and challenging research mission of the National Institute of Child Health and Human Development (NICHD). Our research aims to develop knowledge that will assure that each child is born healthy, wanted, and able to develop to his or her full potential. There is no more fundamental desire of the American people than wishing this for their children. Our guiding belief is that by understanding normal development, scientists will be able to devise treatments for disease and dysfunction in reproduction, birth, growth, and development, or better yet, to prevent these problems from arising.

Infant Mortality and Low Birth Weight

The United States' international ranking in infant mortality is not in keeping with our commitment to the health of our people. This poor ranking (15th) is attributable almost entirely to low birth weight, which is associated with 2/3 of all infant deaths, is twice as frequent among blacks as among whites, and is the preeminent problem in child health in the United States today.

In 1984, the NICHD began a major special initiative: an expanded research program in the prevention of low birth weight. The initiative includes increased research on intrauterine growth retardation (IUGR) and prevention of premature labor, the two factors responsible for low birth weight. As part of this initiative, the NICHD recently funded two new research centers to study fetal growth retardation. We are also aggressively pursuing the causes of premature labor and ways to prevent it. For example, in one clinical trial more than 17,000 pregnant women are being screened for asymptomatic genitourinary infections believed to be associated with premature labor, and studied to determine whether treating these infections will prevent premature delivery. We are also beginning studies of new devices that detect premature labor very early and allow intervention to stop it. Because maternal behavior is such an important factor in low birth weight, our scientists have helped design and fund an intervention study in the District of Columbia intended to identify high-risk women early in pregnancy, encourage them to enter early regular prenatal care, and eliminate behaviors such as smoking and alcohol consumption that increase the likelihood of low birth weight and infant mortality or morbidity.

To provide an ideal system for developing and testing new obstetric and behavioral approaches to managing complicated pregnancies and preventing low birth weight, the Institute recently established a national network of seven maternal-fetal medicine units. A companion network of neonatal intensive care units will provide a setting for clinical trials by neonatologists and nurses to investigate the safety and effectiveness of new treatment and management methods for critically ill infants in improving survival and preventing long-term disability. Since large numbers of patients will be seen through these networks, investigators will be able to evaluate specific drugs or treatments more rapidly, coordinate their findings, and expedite their introduction into practice.

Birth Defects and Genetic Diseases

Birth defects and genetic disorders are a major contributor to infant mortality and lifelong morbidity, but have been unusually difficult to approach experimentally. This situation is now changing due to the new research tools provided by molecular biology, and this field has become one of the most exciting and promising in the Institute. Our intramural and extramural scientists are using animal models to study, at the level of gene structure and expression, the basic processes involved at the earliest stages of development that determine proper or improper organ and limb formation. We are also developing and refining techniques to insert new genes into cells with gene defects, and to control their action correctly. This is the basic research that will lead eventually to human gene therapy. To foster this research, the NICHD recently established a repository where human DNA segments will be collected, stored, and distributed to scientists around the world. The repository will eventually store copies of most of the 100,000 human genes and will enable scientists to locate and easily acquire the specific pieces of human DNA they need to locate genes on specific chromosomes, distinguish normal from abnormal genes, insert genes into chromosomes, and eventually treat genetic diseases.

Sudden Infant Death Syndrome

Once infants pass the critical newborn period, Sudden Infant Death Syndrome (SIDS) is the leading cause of death up to one year of age. The NICHD supports a comprehensive research program to discover the causes and identify the risk factors for SIDS. With the completion of our large cooperative epidemiologic study of SIDS--which, among other findings, provided clear evidence that DPT immunization is not linked to SIDS--our SIDS research program is entering a new phase. A recently issued Request for Grant Applications on SIDS encourages investigators to focus efforts on neural control of cardiorespiratory function, particularly at the brainstem level. We are concerned that scientists in this field have become discouraged by lack of positive findings, and we are determined to rekindle new efforts and approaches to SIDS in enhancing this research program.

Mental Retardation and Learning Disabilities

Mental retardation has been a leading concern of the NICHD since the Institute was established. Much of the nation's research on mental retardation and learning disabilities is conducted in a network of Congressionally established Mental Retardation Research Centers supported by NICHD. Studies in the biomedical sciences supported by the Institute have led to interventions that are highly effective in preventing mental retardation from a few of the many biological causes, such as congenital hypothyroidism. NICHD-supported studies applying the behavioral sciences to the much larger category of socio-cultural-familial mental retardation have suggested that early behavioral interventions may be effective in reducing the likelihood of mental impairment in high-risk infants and children. These studies now need to be validated and extended to include neurodevelopmental stimulation.

The excitement of the "new biology" carries over into the field of mental retardation and learning disabilities as well. Major advances have been made in our ability to study normal and abnormal development of the brain and nervous system, where we must look for the underlying causes of much of the mental retardation and learning disabilities that remains of unknown origin. The new tools of molecular biology are being applied to diagnosing and eventually preventing mental retardation due to genetic defects. A conference that we will convene this fall will provide the Institute with the best advice the scientific community can give as to how best to use these new technologies in our assault on these conditions that prevent children from reaching their full potential.

New Vaccines for Illnesses of Infancy and Childhood

Whooping cough, typhoid fever, and meningitis due to Hemophilus influenzae are still responsible for illness, death, or permanent disability in many children. Fear of side effects from the existing whooping cough vaccine made from whole pertussis bacteria is inhibiting its use, and the disease is returning. NICHD intramural scientists have recently purified the single component of the bacteria that they believe is sufficient to produce an entirely safe and effective vaccine. They are about to start field trials of their new vaccine in Sweden, where without vaccine use pertussis has reached epidemic proportions.

These same scientists have succeeded in developing new vaccines against typhoid fever and H. influenzae. The new typhoid vaccine, just entering field trials in India and Nepal, is expected to have minimal side effects and produce lifelong immunity. Despite effective antibiotics, H. influenzae remains a serious cause of sickness and death in infants and is a leading cause of acquired mental retardation. A recently licensed vaccine based on earlier work of these NICHD scientists is effective in older children but not under two years of age, the time of greatest risk. They have now produced a modified vaccine that is effective in infant monkeys, and we will soon begin a trial in human infants.

Accidental Injuries

Once infancy is past, injuries, not disease, become the leading cause of death and disability. Preventive approaches involve both pediatrics and the behavioral sciences. For example, studies we supported have developed and demonstrated the effectiveness of pediatric office-based interventions to have parents use car seats and seat belts for their children, and lower their home hot water heater settings to prevent scalding. To expand this research, last year NICHD solicited research grant applications on behavioral approaches to injury prevention. We have just begun awarding grants responding to that request.

Population Research

To address developmental problems that appear later in the life cycle, the NICHD supports a comprehensive research program in the population sciences. Goals of this program include devising improved treatments for infertility, and developing safe, effective, alternative methods of family planning. Despite the array of currently available methods, half of the six million pregnancies in the United States each year are unintended, so the need for new contraceptive methods and for understanding people's behavior in risking unwanted pregnancy is evident.

Contraceptive Development

Last year, in testimony before this Committee, the NICHD outlined plans for an increased research program in contraceptive development. Part of that plan included identification of natural products that could be used as contraceptives. I am pleased to report a major achievement in that effort. NICHD-supported scientists have isolated and characterized a protein called inhibin that appears to block a hormonal step necessary for the development of sperm and egg cells. Because inhibin does this without upsetting the body's hormone balance, it may lead to improved contraception for both women and men, and help us to understand some causes of infertility as well. We are also continuing studies of various brain hormones and immunologic aspects of reproduction that have implications for both contraception and infertility.

Unintended Pregnancy

The fact that over half of all pregnancies are unintended despite the availability of effective contraceptives emphasizes the importance of behavioral studies in addressing this problem. A large proportion of the Nation's unintended pregnancies occur among teenagers. NICHD research includes social and behavioral studies focused on factors that may lead to early childbearing. These include studies on initiation of sexual activity and starting and continuing contraceptive use. Several Institute-supported studies have examined factors differentiating sexually active adolescents who regularly use contraceptives from those who do not. Understanding how teens make decisions regarding sexual activity and contraceptive use can provide the basis for developing intervention programs to reduce the number of teenagers who become premature parents.

Contraceptive Evaluation

Over the past year, NICHD-supported researchers have reported major findings about three leading methods of family planning. First, young women who have used oral contraceptives are at no greater risk of developing breast cancer before menopause than are women who have never used them. Coupled with our earlier findings of an apparent protective effect of the pill against some reproductive system cancers, this provides valuable reassurance for the 70 percent of women who have used oral contraceptives at some time during their reproductive years. Second, women who have used IUDs are more likely than other women to become infertile, although the copper-bearing devices most commonly used today are least likely to cause such problems. Third, women who use contraceptive spermicides and unintentionally become pregnant have no greater chance of producing a premature or low-birth-weight infant or an infant with a birth defect than do women who become pregnant while using other types of contraceptives. The link between this program and our research in maternal and child health is readily apparent.

Mr. Chairman, the scientists we support are working in laboratories and clinics around this country on all these problems to bring about the day when our children's futures will truly be limited not by birth defects, mental handicap, or acquired illness and disability, but only by their dreams. With your continued support, we move every year closer to that goal.

The NICHD budget request for FY 1987 is $309,119,000. I will be glad to answer any questions you have.

CURRICULUM VITAE

NAME	Duane Frederick Alexander, M.D.
BIRTH	August 11, 1940, Baltimore, Maryland
MARITAL STATUS	Married Marianne Ellis, Washington D.C., June 23, 1963; two children
EDUCATION	Pennsylvania State University, University Park, Pennsylvania, B.S. Degree, Pre-Medical, 1962 Johns Hopkins University School of Medicine, Baltimore, Maryland, M.D. Degree, 1966
INTERNSHIP	Intern and Fellow, Department of Pediatrics, Harriet Lane Service, Johns Hopkins Hospital, 1966-1967
RESIDENCY	Assistant Resident and Fellow, Department of Pediatrics, Harriet Lane Service, Johns Hopkins Hospital, 1967-1968
MILITARY SERVICE	1968-1970: Surgeon (LCDR), U.S. Public Health Service, and Clinical Associate, Children's Diagnostic and Study Branch, National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, Maryland 1971-Present: From Surgeon to Medical Director, U.S. Public Health Service
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1985-86	Acting Director, National Institute of Child and Human Development, National Institutes of Health
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U.S. INFANT MORTALITY RATE

Mr. **Natcher**. Thank you.

Recently, a great deal of attention has been focused on the high infant mortality rate in the United States which, as you point out, is largely "attributable to low birth weight, which is associated with two-thirds of all infant deaths, is twice as frequent among blacks as among whites, and is the preeminent problem in child health in the United States today."

Nevertheless, Doctor, I believe it is also true that our infant mortality rate is at a record low at this time; is that correct?

Dr. **Alexander**. That is correct, Mr. Chairman.

Mr. **Natcher**. Which are the 14 countries which have lower infant mortality rates than the United States, could you name those for us for the record, Dr. Alexander?

Dr. **Alexander**. The country with the best infant mortality rate based on the data in the 1983 U.N. Demographic Yearbook is Finland with 6.5 infant deaths per 1,000 live births. Second is Japan, 6.6 per 1,000. Those are followed by Sweden, Switzerland, Norway, Denmark, the Netherlands, France, Canada, Spain, the United Kingdom, Australia, the German Democratic Republic, and Singapore. The United States ranked 15th with a rate of 10.9.

Mr. **Natcher**. Thank you.

Is our infant mortality rate going down at the same rate as other countries are, or are we losing ground in relation to other countries?

Dr. **Alexander**. Our rate has been declining at a rate similar to theirs. We suffered a period during the late nineteen fifties and early sixties during which our rate of decline slowed compared to that of other countries.

Since the mid-sixties, we have been on a steady downward trend, at a rate that is roughly parallel to the other leading countries.

TEENAGE PREGNANCY

Mr. **Natcher**. To what extent are infant mortality and low birth weight associate with teenage pregnancy?

Dr. **Alexander**. Teenage pregnancy is much more likely to result in a low birth weight infant and an infant that is more likely to die in the first year of life.

The rate of low birth weight in teenage pregnancy is approximately 10 percent compared to the average of 6.8 percent. An infant born to a teenage mother is also more likely to receive less prenatal care, to receive less adequate care after birth, and has a slightly increased risk of death in the first year of life.

Mr. **Natcher**. Is teenage pregnancy less of a problem in other countries than it is in the United States?

Dr. **Alexander**. Yes, it is. Approximately 13 percent of our births are to teenagers, and approximately 20 percent of our low birth weight births are to teenagers.

INFANT MORTALITY AMONG BLACKS AND WHITES

Mr. **Natcher**. Is infant mortality in the United States declining among blacks and whites at about the same rate?

Dr. **ALEXANDER.** Mr. Chairman, the Secretary's Task Force on Black and Minority Health looked at this very carefully, and in their report on infant mortality and low birth weight, there is a very interesting chart that plots the change in low birth weight and infant mortality over the past 20 years, approximately.

The black and white lines are almost parallel throughout that period of time. The problem is that they are not converging: they ought to be getting closer, but the rates are declining at almost a parallel rate.

Mr. **NATCHER.** When you get the transcript back, Doctor, go into a little more detail for us.

[The information follows:]

INFANT MORTALITY AND LOW BIRTH WEIGHT

The infant mortality rate continues to decline in the United States. During the 1970's through 1981, the overall decline in infant mortality rate was about 4.5% per year and has since slowed to below 3% per year, based upon provisional data through September 1985. The disparity between blacks and whites in infant mortality rate has remained about the same. In 1970 whites had an infant mortality rate of 17.8 per thousand and blacks a rate of 32.6. In 1983 the rate was 9.7 for whites and 19.2 for blacks. The rate among black infants has remained about twice as high as that for whites, and there is no indication that the lines are converging. In recent years the rate of decline in infant mortality has been less in blacks than in whites. For whites from 1980 through 1983, the rate of decline has remained at around 4% per year, while for blacks it slowed to 2% per year in 1982 and 1983. The infant mortality rate is the sum of the neonatal mortality rate (deaths during the first 28 days of life) and the post-neonatal mortality rate (deaths between 28 days of life and less than 1 year of age). The neonatal mortality rate has declined for both blacks and whites through 1983 at approximately the same rate. The post-neonatal mortality rate among whites has leveled off in 1983 and for blacks showed no change in 1982 and an increase of 3% in 1983.

Rates of low birth weight have declined 14% between 1970 and 1983 in the United States. Whites experienced a decline of 17% and blacks a decline of slightly less than 10% over the same time period. In 1970 the rate of low birth weight for blacks was 13.86%, and for whites 6.84%. In 1983 the rate for blacks was 12.59% and for whites 5.67%. The ratio of the black/white difference in the rate of low birth weight in 1970 was about 2, and in 1983 about 2.2. That is, the differential between blacks and whites increased about 10%. Overall the rate of low birth weight has not declined during the last 4 years for whites, and it appears to have increased slightly for blacks in 1983. The rate of very low birth weight, children who weigh 1500 grams or less and who contribute most heavily to neonatal and infant mortality in this country, has remained unchanged since 1970. The rate for whites in 1970 was .95% and in 1983 .93%. For blacks the rate had increased from 2.4% in 1970 to 2.55% in 1983. The ratio of the rate of very low birth weight for blacks over whites, which was 2.5% in 1970, has increased to 2.7% in 1983, suggesting that the lines are diverging.

PREVENTION OF LOW BIRTH WEIGHT INITIATIVE

Mr. **NATCHER.** Talk to us at this time, if you will, about special initiatives, as far as the prevention of low birth weight is concerned.

Dr. **ALEXANDER.** Yes, Mr. Chairman.

Let me try to be a bit brief at this time, and go into more detail later, as you suggest.

Two years ago, the Institute developed a low birth weight prevention initiative. Parts of this initiative focus on intrauterine growth retardation—babies born too small—and parts focus on premature labor—babies born too soon.

We are studying in the two new centers we have established the causes of intrauterine growth retardation-to try to develop means to intervene to prevent it from happening.

We are also trying to determine what causes labor to begin too soon. We have plans to do some investigation with a new device that detects uterine contractions that may start too early, before a woman can detect them herself. This device may enable us to intervene to stop labor when it begins too soon.

We have just established two networks. One comprises maternal-fetal medicine units, that we hope to use for the conduct of clinical trials to evaluate obstetric practices intended to reduce the incidences of low birth weight. The trials will include interventions to try to reduce the incidence of intrauterine growth retardation through nutrition or other means. We also hope to study the management of premature labor and premature rupture of membranes.

We also have studies planned to reduce adverse health behaviors, particularly smoking, drug abuse, and alcohol use, and improve compliance with prenatal care.

I will supply some additional information for the record, Mr. Chairman.

Mr. NATCHER. That would be fine.

[The information follows:]

LOW BIRTH WEIGHT INITIATIVE

In 1985, the NICHD began implementing a major special initiative--an enhanced research program focused on the prevention of low birth weight (LBW) and infant mortality, the most important problems in maternal and child health in the United States today. This effort will continue in 1986 and 1987. LBW infants often require long periods of costly intensive care and have high mortality and morbidity. LBW may be due to intrauterine growth retardation (IUGR), premature labor, or both. The impact of LBW on society is profound. Two-thirds of all infant deaths occur among LBW infants; many of the surviving infants have lifelong physical or mental handicaps. The poor U.S. international ranking in infant mortality is due almost entirely to our higher rate of LBW. Thus the major focus of efforts to reduce infant mortality is appropriately placed on preventing LBW. Components of this initiative include the following:

New Research Centers--Two new research centers supported by NICHD grants are beginning a major effort to understand the causes of IUGR. The studies will attempt to determine ways of predicting fetuses at risk and ways to treat them. One center will concentrate on the mechanisms that control fetal growth in animal models. Investigators will examine the role of growth factors and the supply by the mother of certain minerals, such as calcium and phosphorus, needed for fetal bone production. Concurrently they will initiate a study of pregnant women to determine if maternal bed rest decreases IUGR. Results from this trial will most likely influence the treatment of women suspected of carrying growth retarded fetuses. The other center will direct its major efforts toward the role of nutrition in IUGR. Studies will consider the mother's nutritional status, the transfer of nutrients from mother to fetus, and the fetus' ability to compensate during malnutrition. Researchers will also study the regulation and control of blood flow through the human placenta and its possible role in IUGR. Knowledge will be obtained about the function of the placenta during normal pregnancy and the differences that may be present in IUGR.

Research Networks--The NICHD has also established two networks of research units specializing in neonatal intensive care and in maternal-fetal medicine. The neonatal intensive care network, comprised of seven units, will use cooperative clinical studies to investigate the safety and efficacy of new treatment and management strategies for care of sick newborns. The seven units constituting the maternal-fetal medicine network will study problems in clinical obstetrics, particularly those related to prevention of low birth weight. In both networks, by using common protocols, investigators will be able to study a larger number of patients and provide answers more rapidly than individual centers acting alone.

Epidemiologic Studies--In view of the marked ethnic differences in the rate of low birth weight, particularly the very high rate of very low birth weight among blacks as compared to other ethnic groups in this country, studies are planned to lead to an understanding of the reasons behind the high rate of low birth weight in blacks. Analysis of existing data has revealed that very little of the difference between blacks and whites is accounted for by the currently known major risk factors of low birth weight, namely, maternal age, maternal education, utilization of prenatal care, smoking, drinking, and nutritional status as measured by weight over height. A detailed study of life styles of pregnant women of different ethnic groups is under development to further pursue possible explanations for this difference. Other studies currently planned or under way address possible intergenerational effects which may be related to the risk of low birth weight. Available data suggest that a woman who herself was born low birth weight has a more than twofold increased risk of bearing low birth weight children herself compared to a woman born with a normal birth weight. Preliminary data available at the present time suggest that this is not solely explained by genetic influences.

Special Projects--The low birth weight initiative also includes these special projects and new research activities:

- *Vaginal Infections and Prematurity Study*--A large randomized controlled clinical trial in which women are screened for asymptomatic vaginal or urinary tract infections, thought to cause low birth weight, and treated with antibiotics in an attempt to prevent low birth weight.
- *Better Babies Project*--A study of prevention of low birth weight in the District of Columbia, to determine whether outreach to identify women early in their pregnancy, and link them to existing medical and social services, can reduce the high incidence of low birth weight.
- Research on the mechanism of *initiation of labor*, both prematurely and at term; the pathogenesis and management of premature rupture of the membranes; and the role of fetal growth factors in intrauterine growth retardation.
- A clinical trial to assess the value of routine obstetric *ultrasound screening in detecting and managing intrauterine growth retardation*.
- Studies on the *effects of stress, physical workload, and exercise during pregnancy* on low birth weight, to determine whether excess stress or exercise can cause premature labor, or if an optimal amount of exercise during pregnancy can help prevent premature labor and hence prevent low birth weight.
- Development and testing of an ambulatory tocodynamometer, a device worn by the pregnant woman to *detect uterine contractions of premature labor* and allow intervention to stop the contractions and prevent premature delivery.
- Establishment of *two new research centers* focused on the mechanisms responsible for *premature labor* and its prevention.
- *Intramural NICHD research* on *fetal growth factors* in relation to *intrauterine growth retardation*, and the role of angiotensin receptor abnormalities in *pregnancy-induced hypertension and low birth weight*.

LOW BIRTH WEIGHT PREVENTION

Mr. **Natcher**. Does your special initiative include efforts to prevent teenage pregnancy or is it only directed at women after they are pregnant?

Dr. **Alexander**. We are focusing primarily on prevention, Mr. Chairman.

Mr. **Natcher**. To what extent do you think low birth weight can be prevented by better prenatal care and better living habits by pregnant women?

Dr. **Alexander**. The Institute of Medicine last year conducted a study of low birth weight and interventions that could be targeted toward prevention. The single intervention that would be most effective, based on what we know at this time, is smoking cessation during pregnancy.

Smoking by the mother is a major contributor to low birth weight, and eliminating smoking is the thing we know we could do right now that would be most effective. Prenatal care is also important. There is a correlation between when a woman starts prenatal care and how well she follows the advice she is given, and the weight of her baby.

INFANT MORTALITY RATE COMPARISONS

Mr. **Natcher**. What is the current infant mortality rate among blacks and whites?

Dr. **Alexander**. In 1983, the most recent year for which figures are available, Mr. Chairman, the overall infant mortality rate was 11.2 infant deaths per 1,000 live births. The white rate was 9.7 per 1,000, and the black rate was 16.8 per 1,000.

The current rate of infant mortality is about 10.5 per 1,000. We do not have black-white differentials for any later than 1983.

Mr. **Natcher**. Doctor, why 1983? Why not 1985?

Dr. **Alexander**. The statistical reporting system depends on data supplied by the States, from birth and death certificates. There is a delay between the time that the National Center for Health Statistics receives updated information from the States, and when it is able to supply it.

The Public Health Service is currently involved in efforts to try to speed up that process so we will have more up-to-date information, both for overall infant mortality and for black-white differences.

Mr. **Natcher**. Do we have any new research findings which would explain the discrepancy between blacks' and whites' mortality rate?

Dr. **Alexander**. Mr. Chairman, what we have done is try to separate out various factors that have been associated with black-white differences.

We have looked at the demographic variables, such as socio-economic status, income, and education, and what we have found when we separate all those out is that a black woman is still more likely than a white woman to have a low birth weight infant.

If you take a woman who is in the optimal age range, 25 to 29 years; who has a college education; who begins her prenatal care in the first trimester; who gets good care all throughout pregnancy;

and who does not smoke, the black woman still has a 5.6 percent incidence of low birth weight compared to the white woman's 2.3 percent incidence in that category.

One of the things we are pursuing is a clue on intergenerational effects. Our epidemiologists have demonstrated in the past year that low birth weight tends to repeat itself in subsequent generations,-and we are presently pursuing a study to look at this intergenerational effect as one possible way to account for the black-white difference.

Mr. NATCHER. The birth rate in the United States is continually declining, as you know. How does this trend affect the infant mortality rate?

Dr. ALEXANDER. The infant mortality rate does not depend directly on the birth rate but it depends more on whether that pregnancy is a planned pregnancy or not, how closely it is spaced to the previous pregnancy, and to whom those pregnancies occur.

The highest risk categories are the teenager and the older woman. The older woman is tending to have fewer pregnancies, and the proportion of all pregnancies that occur among older women has declined.

This results in a decline in infant mortality. If we could achieve some of the same declines in teenage pregnancy, our rate would improve further.

NEW VACCINES

Mr. CONTE. Dr. Alexander, welcome before the Subcommittee and to this extraordinary Friday session. We really work hard around here, Doctor.

You preside over an area that is near and dear to my heart, and all reports that come back from the people who deal with the Institute, Doctor, give you high marks and praise, and that is great.

I don't know what you do to make them all happy, but I am glad you are not in politics. I also want to take this opportunity to thank Dr. Haseltine for helping me out with a question I had last year. I certainly appreciate your responsiveness.

Dr. HASELTINE. Thank you.

Mr. CONTE. You mention two new vaccines you are testing, one on typhoid, being tested in India and Nepal. Why would you be testing this vaccine all the way over there, and tell us how many children this has the ability to benefit?

Dr. ALEXANDER. We test the vaccine where the disease is. Typhoid is almost eliminated from this country, but it can affect us when we travel to Nepal or India, and is a problem for the military, which is particularly interested in a vaccine for protection.

The potential is enormous because the attack rate for typhoid in parts of India and Nepal is 1 to 3 percent per year, causing an enormous amount of disability. The vaccine, we believe, has the ability to eliminate this disease.

The disease has no non-human reservoir; it doesn't infect animals, no animal gets typhoid. If we can eliminate it from humans, we can do what we have done with smallpox, and eliminate the disease entirely.

The disease is a major burden for these developing countries, and if we can, through this vaccine, eliminate that disease, we will enable those countries to use their funds for other health purposes.

Mr. CONTE. Do we have a vaccine now for typhoid?

Dr. ALEXANDER. Yes, but it is only 60 to 80 percent effective, and does not give lasting protection. This new vaccine will provide lifelong immunity from one injection at a cost of 10 cents per dose.

H. INFLUENZAE VACCINE

Mr. CONTE. The other is a vaccine for *H. influenzae,* effective for children under 2, who are at greater risk. Where did the development of this vaccine take place, and is this likely to be a vaccine that all children should receive?

How many children do you think would benefit from the successful trial of this new vaccine?

You say it will be tested in a trial involving the entire State of Massachusetts, and I would like you to elaborate on that too.

Dr. ALEXANDER. The *H. influenzae* vaccine was developed in our own laboratories at NICHD by our intramural scientists. What they have done is take a part of the outside coat of the bacteria, what they call a capsular polysaccharide, and use that pure chemical as an immunogen.

The body develops antibodies to that particular chemical which are then protective against an invasive infection from that organism.

H. influenzae causes a number of diseases—ear infections, croup, meningitis, systemic infections, and joint infections. The most serious are the systemic blood infections and meningitis.

There are 15,000 cases a year of *H. influenzae* meningitis in the United States, and one-third to one-half of the children who have this are left with mental retardation or deafness. It is the major cause of acquired mental retardation in this country at the present time.

Our scientists have developed a vaccine that is effective for children over age 2, and that vaccine was recently licensed, and is on the market at the present time. However, it does not work for children under age 2. They don't make protective levels of antibody to it, and we had to trick the body into making antibodies to do that, our scientists bound this particular polysaccharide to the tetanus toxoid, and by doing this, the body makes antibodies to tetanus and the *H. influenzae* organism as well that are protective and probably will provide lifetime protection.

This disease also we have the potential to eliminate. There is no animal that is infected with this disease, so by providing protection against this organism by immunizing all children in infancy, we have the potential to eliminate that disease that is a major cause of mental retardation and illness and disability.

H. INFLUENZAE VACCINE TRIAL

Mr. CONTE. Would you elaborate on your trial for this vaccine?

Dr. ALEXANDER. The *H. influenzae* vaccine is not scheduled for trial in Massachusetts at the present time. It is scheduled for an initial field trial in Sweden, along with our pertussis vaccine. The reason is as follows:

The pertussis vaccine is being tried in Sweden because Sweden has not used a pertussis vaccine since 1979. As a consequence, they are having epidemic pertussis at the present time.

By studying the pertussis vaccine in Sweden, we can get indications not only of antibody formation, but also effectiveness in preventing disease that is prevalent in the community at the time, far more so than in this country.

Since Sweden is not giving pertussis vaccine on its own at the present time, we can employ a control vaccine. The *H. influenzae* vaccine provides a perfect control vaccine. It is given at the same time as the pertussis vaccine would be given, and by using half the children randomized to receive pertussis vaccine, and half to receive *H. influenzae*, we can test two vaccines at the same time, which is very economical, and we can get indications of safety and efficacy for both vaccines.

In Massachusetts, we don't have the same situation. We are giving pertussis vaccine at the present time, and we don't feel it would be ethical to withhold a pertussis vaccine for a clinical trial. Therefore, our design in Massachusetts would be different.

Massachusetts is an almost unique State in that all of the pertussis vaccine used in the State is made by the State Health Department. We have already had discussions with the officials in the State Health Department, and they are eager to cooperate with us in this study.

The design in Massachusetts would be to randomize administration of either the new pertussis toxoid vaccine or the existing pertussis vaccine made by the State Health Department. The distribution would be done by the Health Department in a blind fashion, so we would be able then to compare the efficacy and safety and side-effects of the existing vaccine versus the new pertussis toxoid vaccine, in a perfect setup to do that study.

Mr. CONTE. You say the new pertussis trial will be in Massachusetts?

Dr. ALEXANDER. We are hoping that that will work out.

RESEARCH GRANT AWARD RATES AND PAYLINES

Mr. CONTE. Doctor, in fiscal year 1985, yours was the only Institute with an award rate of less than 30 percent, yet, in terms of pay line, you were only third lowest, after Neurology, and Allergies and Infectious Diseases.

Is that just the vagaries of pay lines at work, or does that mean you get more proposals at slightly lesser scientific merit?

Dr. ALEXANDER. Mr. Conte, the Institute makes its funding decisions based on a percentile system rather than a priority score system, which results in some differences, when comparisons are made among other Institutes that pay by a raw priority score. In fact the Institute has had a steady increase in the numbers of applications received that are of very high scientific merit.

The most indicative figure is the percent of approved grants that are funded.

NICHD paid 28.2 percent of approved grants in 1985.

Mr. **Conte**. How does that award rate compare with your past history of award rates, and what would you say is the effect of going below funding 30 percent of grant applications judged to be scientifically meritorious?

Dr. **Alexander**. The rate has declined steadily from 1981, when we were able to pay 39.2 percent of approved applications. In 1982, the rate was 35 percent. 1983, 34.7 percent. 1984, 29.2 percent. 1985, 28.2 percent.

Mr. **Conte**. That is unbelievable.

Are there private sources of funding which can fill in the gap in the area of child health and human development?

Dr. **Alexander**. There are a number of private foundations that make grant awards for research in areas that relate to some of the same interests as the Institute; the March of Dimes is one notable example, and the Robert Wood Johnson Foundation is another.

They have limited funds, but they do help to fill in some of the gaps.

Mr. **Conte**. You didn't answer me, though, Doctor.

What is the effect of dropping down from 39.2 to 28 percent?

Dr. **Alexander**. The effect is that considerably fewer grants of high scientific merit will be funded for investigators whose applications are in the field of maternal and child health and are assigned to our Institute.

BETTER BABIES INITIATIVE

Mr. **Conte**. Last year, you described the new better babies initiative, a demonstration effort to improve pregnancy outcomes in the District of Columbia, which I believe has the highest infant mortality rate in the country.

What results can you speak of over the past year, and what are the implications of what you have learned and their relevance to programs across the country?

Infant mortality is a big problem in my own Congressional District in the City of Holyoke.

Dr. **Alexander**. The past year has been devoted primarily to putting together the very complex package of prenatal care and developing the outreach system in the target areas of the community.

This package is now in place, and just about ready to go. This involves putting together an enormous complex bureaucracy, ranging from the outreach itself to identify the women early in their pregnancy, to getting them into existing medical care, to providing referral for smoking cessation, for drug abuse clinics, for alcohol abuse clinics, to the WIC program for nutritional supplementation, to social services, or whatever else is needed.

Basically, we are trying to see whether by applying everything we know that is good to try to prevent low birth weight, how much of an impact we can make, on the 16 percent rate of low birth weight in the target area of the city.

Mr. **Conte**. Thank you, Mr. Chairman.

Mr. **Natcher**. Yes, Mr. Stokes.

INFANT MORTALITY

Mr. **Stokes**. Thank you, Mr. Chairman.

Dr. Alexander, let me pick up on the same subject that has been discussed with you by the chairman and Mr. Conte—infant mortality.

If I understand you correctly, over the last 20 years, the gap between the morality rate for black and white babies has remained virtually the same. The lines have never converged, and even though both lines have decreased, the gap between black and white infant mortality rates has remained the same.

Dr. **Alexander**. That is correct.

Mr. **Stokes**. Isn't there also another dimension to this in that the Surgeon General of the United States has issued objectives or goals for 1990. One of those goals is that by 1990 the national infant mortality rate—deaths of children younger than 1 year old—should be reduced to no more than nine deaths per 1,000 live births, with no county, racial or ethnic sub-group having an infant mortality rate in excess of 12 deaths per 1,000 births.

Are you aware of that goal?

Dr. **Alexander**. Yes, sir.

INFANT MORTALITY AMONG BLACKS

Mr. **Stokes**. Haven't we also had a finding by the PHS that the nation will meet the Surgeon General's overall infant mortality goal, but that the goals for these key sub-groups will not be met, especially with regard to black infants?

Dr. **Alexander**. That is correct.

Mr. **Stokes**. Then, of course, that report went on to tell us about many of the jurisdictions throughout the United States where infant morality goals would not be met.

In addition, the Children's Defense Fund has pointed to another problem within this same area. CDF has reported that between 1982 and 1983, the post-neonatal mortality rate—deaths among infants between 28 days and one year of age rose—by 3 percent nationwide, and that not since 1978 has there been a nationwide increase in the post-neonatal mortality rate, and not in 18 years has there been such a large one-year increase.

CDF state that in 1983, older black infants died at a higher rate than the youngest white infants. Are you familiar with those statistics?

Dr. **Alexander**. Yes, sir.

Mr. **Stokes**. So these statistics highlight additional problem areas with regard to infant mortality rates.

Dr. **Alexander**. It does, indeed, one that is receiving intensive examination by the Public Health Service. The Assistant Secretary for Health a little over a year ago established a Special Task Force on Low Birth Weight and Infant Mortality, which monthly has been monitoring these changes, and became aware of this tendency for an increase in post-neonatal mortality. It is of major concern.

We have been looking at this to try and determine, first of all, whether this is just a temporary blip or a continuing trend, and to investigate what factors may account for this seeming slight increase in post-neonatal mortality rates.

Mr. **Stokes**. Do we know the reasons for this alarming situation?

Dr. **Alexander**. At this time, we do not.

Mr. **Stokes**. Has your Institute been able to begin some initial research studies on this problem, particularly relating to black infants?

Dr. **Alexander**. Yes, we have. The efforts that we have made in low birth weight prevention affect particularly the black infant, because of the 2 to 1 predominance of low birth weight among the black population.

The efforts we are making in the networks, the research that we are doing in the vaginal infections and prematurity study, the work with the Better Babies Project here in the District, all of this is really of more pertinence to the black population, because of the heavier concentration of low birth weight among that group.

Mr. **Stokes**. What, in particular, are you doing about this problem?

Dr. **Alexander**. We are trying to get at what accounts for the difference, and to find out what kind of interventions are effective in reducing low birth weight among both black and white infants.

As I mentioned earlier, we also are pursuing intergenerational effects. Dr. Berendes has had discussions with people at Meharry, in particular, about whether we can get information from black families that have been at middle or upper socio-economic levels for two or more generations, and look at low birth weight incidence among that population, to see whether this intergenerational effect is sufficient to account for a sizable portion of the discrepancy.

We also are looking at the data that show that at all low birth weights, the black infant survives better than the white infant. The other data that we have, and Dr. Berendes may comment further on this, if he would like, indicate that at all gestational ages, the black infant, when tested, is more mature physiologically than the white infant.

So there may, in fact, be some specific racial difference, so that low birth weight is not as detrimental for the black population as it is for the white.

There may be a difference such as that the normal duration of pregnancy. In the blacks it may be not 40 weeks, but 39 or so weeks as compared to the whites. These are the kinds of things we are looking at.

SMOKING IN WOMEN AND THE EFFECTS ON BABIES

Mr. **Stokes**. We are reading a lot now about the increase in smoking among women. Have you conducted any studies on this increase in smoking among women and the effect it is having on new-born babies?

Dr. **Alexander**. We have done a number of studies. We did studies several years ago which indicated that on the average a woman who smokes decreases the weight of her baby about half a pound. The more she smokes, the more the decrease in birth weight. NICHD epidemiologists reported a study just this year that indicated not only does smoking affect the weight of the baby, it also has an effect on how much too early that baby is born.

The woman who smokes is 60 percent more likely to deliver a baby eight or more weeks early than the woman who does not smoke. So we now have evidence there is an effect not just on the weight of the baby, but on the premature delivery of that baby as well.

ORAL CONTRACEPTIVES

Mr. STOKES. Doctor, what are your most recent findings with regard to oral contraceptives and other methods of birth control?

Dr. ALEXANDER. The oral contraceptive as presently formulated is an extremely safe and effective method of contraception. A study that our scientists reported just this year is a study on the oral contraceptive in relation to breast cancer.

There had been concerns raised about whether oral contraceptive users were at an increased risk for developing breast cancer. Based on the results of a study developed by our Contraceptive Evaluation Branch, results indicated women who use oral contraceptives are no more likely than non-users to develop breast cancer prior to menopause. We will be following up this study to look at post-menopausal effects, as well.

Previous studies that we conducted demonstrated not only the safety of the oral contraceptive but also some protective effects of oral contraceptive use as well.

For example, women who use the oral contraceptives are less likely to develop endometrial cancer or ovarian cancer than women who are non-users. We believe it is important to do these studies and bring them to the attention of the public because a major reason that women give for not using oral contraceptives and having an unintended pregnancy as a consequence is fear of the safety of the contraceptive methods available.

Thus, we think it is very important to do these studies and, when they do demonstrate safety or risk, to get that information to the public.

Mr. STOKES. Have you initiated any clinical trials regarding this?

Dr. ALEXANDER. We are planning a clinical trial for 1987 on oral contraceptive use in relation to cardiovascular disease. This will test the new formulations of oral contraceptives and look at cardiovascular disease in users of present day oral contraceptives compared to those of former years.

TRANSMISSION OF AIDS VIRUS THROUGH HUMAN MILK

Mr. STOKES. I noticed in your budget justification that the AIDS virus may be transmitted to infants during feeding through human milk. Can you tell us something about this finding?

Dr. ALEXANDER. There has been to my knowledge one case report of an infant who was born free of AIDS and had no means of acquiring AIDS at birth. The mother subsequently received a blood transfusion, acquired AIDS as a consequence, and the infant also developed antibodies to the AIDS virus.

The AIDS virus was demonstrated in the mother's milk and the presumption was the infant may have acquired the AIDS virus from breast milk. We do know that the AIDS virus is in breast milk.

There is also evidence that antibodies to the AIDS virus are in breast milk. We are presently trying to evaluate this route of transmission for AIDS. It is not totally clear at this time.

Mr. STOKES. Thank you, Doctor.

Thank you, Mr. Chairman.

INFANT MORTALITY RATES

Mr. NATCHER. Dr. Alexander, is the infant mortality rate highest among groups who have the highest birth rates?

Dr. ALEXANDER. The infant mortality rate does increase with the number of pregnancies that a woman has. Particularly when you get to four or five pregnancies, the likelihood of infant mortality and low birth weight both increase.

PREVENTION OF UNWANTED PREGNANCIES

Mr. NATCHER. Now, under prevention of unwanted pregnancies, Doctor, you state, and I quote, "half of the six million pregnancies in the United States each year are unintended so the need for new contraceptive methods and for understanding people's behavior in risking unwanted pregnancies is evident."

How do you know that half of the pregnancies are unintended, Doctor?

Dr. ALEXANDER. This information is based on survey data and on data about the number of abortions. We know, for example, that there are approximately 1.5 million abortions in this country each year. These account for a substantial portion of the unwanted pregnancies.

You also can survey women who have just given birth and ask them whether they wanted this pregnancy at this time or wanted the pregnancy at all. Based on those responses we have put together data that give a clear indication of the extent of unintended pregnancy. The latest figure is 52 percent of pregnancies are unintended—that is either unwanted at all or unwanted at the time they occur.

Mr. NATCHER. How long has your Institute been working on this problem?

Dr. ALEXANDER. We have been working on it since about the time that the Center for Population Research was established in the Institute. This goes back to about 1969.

Mr. NATCHER. Do you think you have accomplished something by virtue of this work, Doctor, of some significance?

Dr. ALEXANDER. We have, sir. We certainly haven't solved all of the problems. However, our research has contributed to the development of new and improved contraceptive methods, and has contributed to people's use of them by demonstrating their safety. We have gotten behavioral data that indicate how people make choices about use or non-use of contraceptives and why they make the choices that they do. This information has been useful in implementing some of the family planning programs. We have a long way to go.

INHIBIN AS AN EFFECTIVE MALE CONTRACEPTIVE

Mr. **Natcher**. Yes. How long will it take to determine whether inhibin is an effective male contraceptive, Doctor?

Dr. **Alexander**. That is very difficult to say, Mr. Chairman. We have just isolated, purified and characterized the structure of this substance within the past several months. We are taking steps to make this substance available to the scientific community for broad scale investigation.

The initial studies, of course, will be done in animals to investigate futher its specific physiological effects and just exactly how it works, whether it will, in fact, have the intended and expected effects. Then it will be a matter of developing a formulation of this substance that will be useful and effective in humans.

It will be several years before we are even ready to go to human studies. In general, from the time that you identify a substance like this until the time, if everything goes well, that you can be on the market with a product, is from eight to ten years.

VACCINE DEVELOPMENT

Mr. **Natcher**. What is the division of responsibility between your Institute and the National Institute of Allergy and Infectious Diseases with respect to vaccine development, Doctor?

Dr. **Alexander**. Most of that responsibility lies with the National Institute of Allergy and Infectious Diseases. We have one intramural Laboratory of Developmental and Molecular Immunity that looks at immunity from a developmental standpoint, that is how the immune system develops, why it is able to respond to certain antigens at certain periods in the life span and not able to do so in others, and what specific antigens in an organism will stimulate immunity.

This research has led them to their work in vaccine development in specific areas. They have followed some of the leads that they have developed, and this work has led them to the work in pertussis, hemophilus influenzae, typhoid, and meningococcus vaccine development. It is clear that the primary responsibility for vaccine work lies within NIAID.

PERTUSSIS VACCINE

Mr. **Natcher**. Which institute is funding the field trial of new pertussis vaccine?

Dr. **Alexander**. There are three pertussis vaccines at least that are going to be tested simultaneously in Sweden. NIAID is funding trials of two Japanese vaccines. One is an acellular vaccine that is basically a supernatant of the culture of the pertussis organism.

The second is a toxoid vaccine that is produced by a chemical detoxification. Those are the trials in Sweden that are being funded by NIAID.

The study that we will be doing is limited to Goteborg in Sweden. It will be funded partly by NICHD and mostly by Sweden. It will be testing a different type of toxoided vaccine that is toxoided by a new and unique process.

The Government will hold the patents to this process and will be able, if this vaccine works, to issue a license for the manufacture of this vaccine that will be a U.S. product and that will help to hold the cost down.

POPULATION RESEARCH

Mr. NATCHER. The President of the Planned Parenthood Federation told us this morning that population research receives low priority at NIH because NIH is mainly disease oriented, whereas research of this type mainly benefits healthy people. How would you respond to that, Doctor?

Dr. ALEXANDER. Mr. Chairman, I don't think that population research in any way receives low priority at NICHD or at NIH. We try to balance our programs.

We respond to where the problems and opportunities are. We have made special efforts to stimulate research in contraceptive development, and in understanding population change. We have two major initiatives in the Institute at present, one in low birth weight prevention and one in contraceptive development, so that we have maintained population research as an equal component with the research for mothers and children.

USE OF CONTRACEPTIVES BY WOMEN

Mr. NATCHER. We understand that one of the reasons women do not use contraceptives is fear of possible side effects. Are such fears justified, Doctor?

Dr. ALEXANDER. Only in some instances, yes, Mr. Chairman. The most recent example is the intrauterine device. The results reported this year by our Contraceptive Evaluation Branch demonstrated that some types of the intrauterine devices had an unacceptably high risk of subsequent unwanted infertility. These devices are not in use any longer and, in fact, even the device that was demonstrated to have the least adverse effects, and really no adverse effect at all on infertility in the woman who had already had a pregnancy, has now been withdrawn from the market as well.

With regard to oral contraceptives, the research that NICHD supported on earlier formulations of oral contraceptives in particular pointed out hazards for certain groups of women using the pill. These groups included women who were smokers, women who had preexisting cardiovascular disease, and older women.

As a consequence of this information, formulations have been modified and warnings have been issued that the pill is really inappropriate for certain groups of women.

Mr. NATCHER. Mr. Conte, I yield to you.

RESEARCH NETWORKS ON LOW BIRTH WEIGHT PREVENTION

Mr. CONTE. Thank you, Mr. Chairman.

Doctor, last year we talked about a new program you were initiating, funding two research networks on low birth weight; one, a network of six maternal fetal medicine units, the other, a network of six neonatal intensive care units. Did you establish those networks and, if so, please provide a list for the record of the recipients and the size of the awards.

Dr. Alexander. Mr. Conte, we will be awarding those grants this month. We are funding those units and we will be bringing the investigators from those units in for meetings with NICHD staff to begin to identify topics for the clinical trials in those units and to implement those trials.

Mr. Conte. Are they similar to the purpose of the general clinical research centers: a place where you have controlled clinical trials that can be carried out?

Dr. Alexander. They are, but they go a bit beyond that. The general clinical research centers in general do not function as a network, and admit patients only for research. They provide a focus for clinical research within that setting and for clinical trials, but what we plan to do here is different. Our units will be in regular obstetric clinics and neonatal intensive care nurseries. We will use them as a place for conducting clinical trials that will involve the same protocol at each of the units so that we can obtain large numbers of patients relatively quickly, use the same protocol on all, and get answers relatively rapidly to the questions that we are asking.

The model is much closer to the networks that have been used successfully for a number of years by the National Cancer Institute to test new methods of chemotherapy.

Mr. Conte. You are going to get that other stuff for the record.

[The information follows:]

Maternal-fetal medicine units

Institution:	FY 1986 Amount
University of Southern California Medical Center, Los Angeles, CA	$32,319
Northwestern Memorial Hospital, Chicago, IL	28,710
Columbia University, New York, NY	46,055
Magee-Womens Hospital, Pittsburgh, PA	21,763
Johns Hopkins University, Baltimore, MD	25,126
Yale University, New Haven, CT	43,996
University of Tennessee, Memphis, TN	18,288
Total	216,257

Neonatal intensive care units

Institution:	FY 1986 Amount
University of Alabama at Birmingham, AL	$31,926
University of Texas Health Science Center, Dallas, TX	23,825
University of Miami, Miami, FL	31,045
Wayne State University, Detroit, MI	24,587
Case Western Reserve University, Cleveland, OH	33,266
University of Vermont, Burlington, VT	31,503
University of Tennessee, Memphis, TN	24,605
Total	200,757

Mr. Conte. These are all going to be funded in the cooperative agreement line?

Dr. Alexander. They are all cooperative agreements.

Mr. Conte. How does the cooperative agreement line make out in the FY 1986 revised budget and fiscal year 1987 budget proposal?

Dr. Alexander. These will be a type of cooperative agreement that is included with the regular research grants. In that line in the 1987 budget our total number of grants will be 456 new and competing awards, almost equivalent to the revised 1986 level.

INTRAMURAL INFERTILITY CLINIC

Mr. CONTE. Tell us about some of the work you have been doing particularly in the intramural program. How many people do you treat, would you say? Are they couples who may have tried other treatments without success? Do you end up being able to help some of them? This is in the field of infertility.

Dr. ALEXANDER. We have a major research effort in infertility in the intramural program. One of the success stories we are proudest of has been in treating men with a condition called hypogonadotropic hypogonadism. This condition is caused by lack of a hormone from the pituitary gland that is needed to stimulate spermatogenesis.

We have been able to replace that missing hormone, to provide stimulation for the testicle to produce sperm. By the latest count, we have 28 infants born from this program to men who were previously infertile.

Mr. CONTE. Is this at the Institute?

Dr. ALEXANDER. This is in the NICHD intramural program.

Mr. CONTE. I was at the Cleveland Clinic recently reading their brochure and they have a tremendous record up there. I imagine it is the same process.

Dr. ALEXANDER. It may be the same condition, sir. I am not sure.

Mr. CONTE. You can elaborate on this for the record. I am interested in it.

Dr. ALEXANDER. I will be pleased to do that.

[The information follows:]

NEW CHILD HEALTH BUILDING

Mr. CONTE. Last year we received your report on the need for a new child health building, which has been in the planning phase since the late 1960s. I guess we can call this the orphan child. It was envisioned in the authorization of the Child Health Institute back in 1962.

I thought last year's report made a very convincing case for the need for this building and with the Chairman's permission I would like to include a copy again in this year's hearing record.

Hearing no objection, I will put it in.

[The information follows:]

NICHD MALE INFERTILITY CLINIC

NICHD intramural scientists have been successful in developing an effective treatment for a type of male infertility that had long been resistent to treatment. This type of male infertility—hypogonadotropic hypogonadism—is caused by the pituitary gland's failure to produce enough of the hormones that regulate the production of sperm and the male sex hormone testosterone. Affected men not only fail to produce sperm but they are often sexually immature as well. Due to nearly a decade of study into the hormonal requirements of male reproductive function, NICHD scientists were able to devise a treatment regimen that virilizes and induces fertility in these patients. The success of the treatment is dependent on a carefully regulated and timed administration of the lacking pituitary hormones. Using this therapy, 43 babies have been fathered by these patients in the NICHD Male Infertility Clinic. The success of this treatment has prompted other clinicians to adopt it, and it is now being used in many male infertility clinics around the country.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

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Proposed NICHD Building

Thomas E. Malone

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Deputy Director, NIH

March 1985

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Executive Summary

In House Report No. 98-911, the Committee on Appropriations requested that the NIH prepare and submit a report on the current NICHD facilities, the need for a new building, and an outline of the plans for that building (p. 79). The following is submitted in response to that request.

The NICHD was established in 1962 as a reflection of the concept that while we continue to search for solutions to specific disease problems, we must also probe deeply into all of the life processes which determine normal or abnormal human development. Since the Institute's establishment, NICHD research has contributed to a very significant decrease in infant and maternal morbidity and mortality. However, the NICHD intramural research program has always been conducted largely in shared or leased space which is dispersed among 12 separate buildings. In this space, the NICHD is able to provide an average of only 141 square feet for each of its intramural scientists and support staff, as compared to an NIH average of 240 square feet. These conditions impair the ability of the NICHD to recruit and retain outstanding scientists as well as result in inefficiencies in the research effort.

Many facets of the NICHD program would benefit from the consolidation of its staff and equipment into one facility. A new building would provide for maximum utilization of expensive equipment items that, despite efforts to share the equipment, often is duplicated because the program is so widely dispersed. The new building would enhance the ability of the NICHD to comply with the new guidelines set for animal welfare. In addition, centralization of administrative and support personnel would provide for a more efficient working environment. The most important benefit to current operations would be the enhanced communication among NICHD research staff. A collection of the separate elements into a single facility would stimulate many new and exciting scientific efforts, and increase the productivity of current research endeavors.

Other components of the NIH, as well as the NICHD, would benefit from the new building. The new facility would create state-of-the-art resources which would serve the entire NIH, including a centralized, highly efficient facility for the micro-analysis and synthesis of individual genes and proteins (to be used, for example, in "gene therapy" and in the development of more effective contraceptives), and a facility for the use of entirely safe, nonradioactive isotopes in the diagnosis and treatment of serious childhood diseases. It would also enable the NICHD to vacate most of its current space on campus, thus creating the opportunity for scientists in other Institutes to return to the campus from leased and distant space (e.g., the Park Building in Rockville). Giving up leased space will eliminate the annual rental of

Proposed NICHD Building

$625,000 now paid for space in the Park Building. Moreover, space that NICHD has shared with other Institutes would be returned and used to relieve over crowding in all of the other NIH Institutes.

The proposed building would support the current intramural research program; it would not be designed to enlarge that program. The building would contain 88,000 square feet of net space, and provide for NICHD's intramural biomedical research efforts, tissue culture and containment facilities, animal quarters, and central administrative and support facilities.

The construction of this laboratory building is estimated to cost about $57.1 million and would take approximately three years to complete. The funds could be provided in three stages (Year 1--$15.1 million; Year 2--$30 million; Year 3--$12 million).

Proposed NICHD Building

Introduction

In its report on the Fiscal Year 1985 budget for the Department of Health and Human Services, the Committee on Appropriations stated:

> "The Committee is concerned by the continuing dispersal of the programs of the NICHD in 12 separate buildings on the NIH campus and in leased quarters.
>
> As part of the FY 1986 budget submission, the Committee expects the administration to request construction funds, which are estimated at $60 million in total. In addition, the Committee requests the NIH to prepare a summary report, in time for next year's hearings, on the current facilities, the need for a new building, an outline of the plans for that building, and its estimated cost, and ways in which the needed funding can be provided over a period of two to three years." (House Report No. 98-911, page 79).

The following report has been prepared by the National Institutes of Health of the Department of Health and Human Services in response to this request.

Background

In 1961, a task force report to the White House charged that research into the physical, intellectual and emotional growth of the child was "severely handicapped" by the absence of a central coordinating point. It called for a new Institute at the National Institutes of Health to launch a "concentrated attack" against disorders of human development. The task force believed that solutions to problems of physical and mental development had to be based on a better understanding of normal human biology and behavior. At the time, by law, each Institute was designed to wage a battle against a specific disease. The Congressional mandate had no provision for an Institute with a major interest in normal human reproductive, growth, and developmental processes. Therefore, in 1962, a totally different pattern of research effort was set in motion at the NIH through legislation which authorized formation of the National Institute of Child Health and Human Development. The NICHD's creation symbolized an emerging concept: While we continue to search for solutions to specific disease problems, we must also probe more deeply into all of the life processes--behavioral and biomedical, normal, and abnormal--as a basis for maintaining health as well as for the prevention and conquest of disease.

Over the past two decades, NICHD research has aimed to assure the birth of healthy babies through basic and applied investigations on normal and abnormal fetal development and on the problems of pregnancy. Many studies have sought to assure the birth of wanted babies through studies on human fertility and infertility, better methods of family planning and contraception, and adolescent childbearing. Still other NICHD research has aimed to provide all children the opportunity for productive and healthful adulthood through efforts to understand the causes of mental retardation, birth defects, and learning disorders, as well as normal development and growth. The results of this research indicate that the key to the prevention of common "adult" diseases such as cancer, heart disease, hypertension, psychiatric disturbances, diseases of the immune system, neurological disorders, and premature aging, lies in our understanding of the phenomena that govern early development. Through NICHD research, we ultimately hope to learn what sets the stage for adult diseases and how to prevent these diseases at conception and during early development. Already, research supported by both the intramural and extramural programs of the NICHD has contributed to a 50% drop in infant mortality in the U.S. since 1962, and an 80% drop in the maternal death rate from pregnancy and childbirth in the same period. NICHD research has also contributed to the prevention of many types of mental retardation.

At the time of the original NICHD authorization, it was planned that a building would be constructed on the NIH campus to house the Institute's intramural research program. However, since its inception in 1962, the NICHD has been dispersed among 12 separate buildings scattered within a two mile radius of the Clinical Center, the focal point of NIH research. The proposed NICHD building would greatly increase the likelihood that the intramural program will fulfill all of its abundant potential. It would permit scientific and administrative efficiencies now prohibited by the physical fragmentation of programs. In addition, a modern building would enable scientists to pursue sophisticated research that is increasingly difficult to perform with obsolescent facilities now being used.

Current Facilities

According to the most recent NIH space survey (March, 1983), the NICHD provides an average of 141 square feet for each of its intramural scientists and support staff, as compared with the average for all Institutes of 240 square feet. There are many places in the NICHD where individuals have no facilities to house animals, where several people share a single desk, and where scientists must "rotate shifts" to obtain working space. Moreover, the Institute is fragmented over a wide area. The space management survey mentioned above identified 12 different buildings which house about 430 NICHD research personnel. Adjusting that survey for buildings which are adjoining and connected, NICHD staff work in seven different physical locations, each separated from the other on the campus by a 15-minute walk. In addition, some of our scientists work in rental space requiring travel by car. The new NICHD Primate Center in Poolesville, which must be located in a rural setting, is the only necessary separation within the NICHD program.

In addition to being crowded and scattered, NICHD people are housed, in some cases, in space rejected earlier by other Institutes. For example, the Laboratory of Developmental Neurobiology and the Laboratory of Neurochemistry and Neuroimmunology, which together comprise one of the world's strongest programs in developmental neurobiology, occupy space largely in the basements of Buildings 35, 36, and 37. The laboratories were created out of space that was originally intended to function as a utility exit, to be used primarily for the delivery of mail and supplies. It is very difficult to pursue high quality research on sterile tissue culture systems because this space opens directly into the air flow from the loading dock and the dumpster. The configuration of this laboratory space also makes heating and air conditioning inadequate for research purposes.

Many NICHD laboratories are located in buildings that have been in use for approximately 40 years without modernization of support systems and architectural features. Today's advanced research requires very precise temperature and air purity controls that are extremely difficult to achieve in outmoded facilities. There is a growing concern that the quality of research the Institute conducts will begin to suffer and that it will become difficult to recruit and retain high caliber researchers to work in these inadequate facilities.

Need for New Building

The original plans envisioned the building "to make possible" the operation of an NICHD intramural program. While the scientific and administrative staff of the Institute have succeeded in maintaining an excellent research program under difficult conditions, it is doubtful they will be able to continue to do so. The need is now greater than it was in the 1960s and the rewards of such a facility are more certain since it will house a program of proven excellence in an atmosphere where it can consolidate and flourish. The subsequent paragraphs describe the benefits to current NICHD operations, research initiatives, and benefits to other parts of the NIH that would occur with the new building.

Benefits to Current Operations

The benefits of a new building to house the NICHD program are many, as listed below:

a. Dollars and space.

At the present time the program maintains, and must periodically replace, large numbers of expensive, duplicative items of scientific equipment. A centralized facility would enable more sharing of sophisticated instruments than is currently possible in the widely dispersed program. For example, each Laboratory has a number of high-speed centrifuges ($40,000 each). These are used at frequent, daily intervals, but not continually. A central centrifuge facility would permit substantial savings.

Similarly, whereas we now maintain nine dark rooms (in addition to those shared with other Institutes), a centralized dark room with a single automated film developer would allow maximal utilization by Institute personnel and save much space and money.

A common electron microscope facility would allow the consolidation of three, now separate but extensive facilities. The provision of a centrally located high-speed computer capability is highly desirable; it would permit savings of both space and money, as well as more efficient use of pooled computer expertise. Such examples are numerous. Even such small things as shared projection equipment or central stationery stores would result in worthwhile economies in space and dollars.

b. Personnel.

A great deal of administrative and support effort could be saved through the consolidation of the program. A centralized typing pool could be organized. The program's messengers could be assigned to other duties, the glass-washing staff could be utilized more efficiently, the ordering staff could be consolidated, and the administrative staff would save the many hours they spend each week traveling from one building to another.

c. Animal facilities.

After extensive engineering and architectural consultation, we have determined that it would be very difficult to bring the Institute's present animal quarters into compliance with the new guidelines for animal care. A new building with animal facilities built to meet these new guidelines would facilitate consolidated animal care from support staff as well as centralized ordering and surveillance.

d. Facilitation of science.

Perhaps one of the most important benefits of a consolidated facility would be in terms of the enhanced communication among Institute staff. A most vivid example is in the areas of neurobiology and molecular biology. The NICHD Laboratory of Molecular Genetics is one of the finest collections of world-class molecular biologists at the NIH or in the world. It is headed by Dr. Igor Dawid, a member of the National Academy of Sciences. The NICHD neurobiology program, as mentioned before, is strong and progressive. It is the case, however, that the advances in neurobiology that are most valuable in basic and clinical terms in recent years have been in the area of molecular biology. Under current conditions, an NICHD post-doctorate fellow in neurobiology who undertakes projects with someone in the molecular biology area must make a 30-minute walk back and forth between the two laboratories. In terms of more productive interaction between scientists, the benefits of locating these programs in a single facility are obvious.

A similar case could be made for the conjoining of the Laboratory of Theoretical and Physical Biology with the Laboratory of Developmental and Molecular Immunity. This latter laboratory, under the guidance of Dr. John Robbins, is concerned with basic and practical investigations of vaccine preparation, particularly the pertussis vaccine. For this purpose the purification and evaluation of various antigens is required. In the LTPB, there is one of the world's foremost experts in protein purification by gel electrophoresis, Dr. Andreas Chrambach. Although there is now an interaction between these groups, a closer laboratory relationship would certainly facilitate production of a safe pertussis vaccine for use in infants.

Examples of such useful advantages for both training and research can be found throughout the NICHD program. Collection of several elements into a single facility would stimulate scientific effort on many fronts. These benefits, although not as easy to quantify as those in terms of dollars and square feet saved, may have an even more wide-ranging effect.

Initiatives

This new facility presents the opportunity to maximize the capabilities of the present staff and to create state-of-the-art, NIH-wide resources under the umbrella of the NICHD. Among these would be the following:

NICHD presently has the expertise to develop a centralized, micro-analytical facility that would permit the analysis and synthesis of individual genes and proteins. Current staff includes Dr. Harry Chen and Mr. John Morrell who are considered to be the best peptide chemists at the NIH. They are now working in space some several miles from the NIH. Dr. Chen, Mr. Morrell, and their associates are completely capable of constructing and operating a microchemical facility consisting of protein microsequenators, mass spectrometers, DNA synthesizers, and laboratory computers which would allow a broad range of molecular operations from the construction of peptide analogs of reproduction-controlling hormones (the goal of which is to produce more effective contraceptives), to the construction of synthetic genes to be employed in the eventual "gene therapy" of human genetic disorders. In addition, this facility would provide an NIH-wide resource for the performance of comparable tasks for other Institutes. Such a microchemical facility provides an enormously sensitive and powerful approach toward the solution of a variety of difficult problems in molecular and developmental biology, as well as a resource for the design of clinical tools. Such a facility exists at several universities, but not as yet at the NIH.

Proposed NICHD Building

NICHD scientists presently have the expertise to develop an up-to-date pilot plant for the production of bacterial and viral reagents on a macro-scale. The Laboratory of Developmental and Molecular Immunity, under the direction of Dr. John Robbins, is in the forefront of the nation-wide effort to develop a completely safe pertussis vaccine. The initial studies, using Dr. Robbins' unique approach to the problem, look very promising. The new NICHD facility would provide an NIH-wide resource for production of this and other vaccines, as well as for the macro-scale collection of hormones, growth factors, and other clinically important materials from cultured mammalian cells.

NICHD scientists also have the expertise to develop an up-to-date facility for the intensive study of non-invasive, non-radioactive methods for the diagnosis and possible treatment of childhood metabolic diseases. Dr. Alfred Yergey of the Laboratory of Theoretical and Physical Biology is one of the leading figures in the effort to deal with clinical problems using entirely safe, non-radioactive isotopes. Dr. Yergey's recent studies have allowed us to determine the metabolism of calcium in children using an innocuous stable isotope and mass spectrometry, and his current studies give promise of yielding information on the metabolism of carbohydrates in various children's nutritional diseases without the necessity of assaulting the children with radioactivity. The new NICHD facility would provide the opportunity to enlarge this effort in mass spectrometry and to explore fully the potential of these new analytical tools for therapeutic advantage.

Benefits to Other Parts of NIH

Because of a shortage of laboratory space on the NIH campus, several intramural programs have long been located in leased facilities off campus. Currently scientists from NICHD, the National Cancer Institute, the National Institute of Dental Research, and the National Institute of Neurological and Communicative Disorders and Stroke are housed in the Park Building, about five miles from the NIH campus. Not only would the new NICHD facility provide space to consolidate its investigators on the campus, but part of the campus space relinquished by NICHD in moving to its new building would be used to return scientists from the other three Institutes as well. This consolidation of research would be of significant value to the three Institutes and would eliminate the annual rental of $625,000 now paid for space in the Park Building. Moreover, other space that has been used by the NICHD on campus, as well as off-campus, will be made available to relieve overcrowding in virtually all of the other Institutes.

Outline of Plans for the Building

The size of this building is about the same as planned originally--approximately 88,000 square feet of net space. This would house the Institute intramural research effort (about 70% of the space). The tissue culture and containment facilities would utilize about 5% of the space; the animal quarters, some 10%; and the central administrative and support facilities approximately 15%. The building would permit better working conditions, with the size of the intramural program remaining at its current level.

Cost of the NICHD Facility

The NICHD facility (Building 33 on the NIH master plan, at a site near the Clinical Center) was originally designed in 1969. In 1979, the cost of construction of the building and its associated parking structure was estimated at $37 million. Last year, at the request of the Congress, a rough estimate of $60 million was given as the cost in FY 1986.

In the FY 1985 appropriation for Buildings and Facilities, the Congress included $500,000 for a thorough updating of the building design. Examination by our architects and engineers, together with program officials, has determined that while the size of the building as originally planned is still appropriate, the shape (four wings around a center court) is no longer optimal for the current NICHD research programs. The original design was predicated on the need for clinics, prior to the construction of the Ambulatory Care Research Facility in the Clinical Center. It also allowed more office and primate-holding space than is currently required. However, the laboratory space originally allocated is inadequate for the current program. Providing for present needs within the building as designed would probably cost a total of about $68.5 million. However, a redesign into the shape of a more conventional laboratory building (such as a smaller version of Building 37, the National Cancer Institute's principal laboratory building) would provide for more efficient utilization of space and reduce both construction and operating costs. An estimated $57.6 million would be required for redesign and construction. NIH is pursuing this option by taking initial steps to engage a construction manager and architect/engineer firm.

Phasing of Construction

Construction of a large, complex laboratory building normally takes several years, and funds could be provided in three stages, as follows:

Year 1--$15.1 million

This would provide for bringing utility lines (steam, chilled water, electricity, etc.) to the site; the design update and construction of the parking structure, which for logistical reasons should precede construction of the building itself; site excavation; and concrete work, including footings, foundations, frame and floors.

Proposed NICHD Building

Year 2--$30 million (approximate)

This would provide for completion of the shell of the building; installation of stairwells, elevators, utility risers and major duct systems; construction of access roads; and purchase of items with a long lead time, such as a chiller for the central air conditioning plant, large fans, pumps and electrical switch gear.

Year 3--$12 million (approximate)

This would provide for interior finishing; installation of laboratory benches, hoods and fixtures; installation of autoclaves and equipment for animal facilities; completion of electrical and other utility systems; and landscaping the site.

Summary

The NICHD intramural research program, which has achieved great stature, is conducted primarily in borrowed or leased space and is dispersed among 12 widely separated buildings. This space is poor qualitatively, and inadequate quantitatively, by NIH standards. These conditions threaten the quality of research that can be conducted, impair the ability of the NICHD to recruit and retain outstanding scientists, and result in inefficiencies in the research effort. In addition to conserving funds and personnel, a single NICHD facility would stimulate many new and exciting scientific efforts, and increase the productivity of current studies. Other Institutes of the NIH would benefit from the new building because state-of-the-art resources could be created which would serve the entire NIH. Moreover, the NICHD would vacate its current space on campus, thus relieving overcrowding in all of the other Institutes. The proposed building would support the current intramural research program, but would not enlarge that program. The construction of this 88,000 square foot laboratory building would cost about $57 million, and the funds could be provided over three years.

PLANS FOR THE CHILD HEALTH BUILDING

Mr. Conte. We provided about $500,000 to update the plan for the building back in fiscal year 1985, which resulted in the report we were talking about. As we followed the issue this year, it was my understanding that a figure somewhere in that same ball park was included in the Institute's budget proposal to do the actual updating of the architectural plans and drawings, and that it was in this budget—at least when it got to the Secretary's level.

Is that accurate and did that proposal get dropped after the budget left HHS, along with so many other things?

Dr. Alexander. The $500,000 that was provided by this committee in fiscal year 1985 for updating the design remains available. The progress has gone forward with planning for that building.

At the present time we are rethinking just what purpose that building could best serve. We have had discussions with the various people involved.

We feel that the best function for that building at the present time would be a building that would not only consolidate the NICHD intramural program, but serve some other purposes as well. We have evolved into having a much larger neuroscience program in the Institute. Since the NICHD building was originally designed, there has been built on the NIH campus at the clinical center an ambulatory care research facility that provides the outpatient clinic services that were formerly envisioned in the NICHD building. As a consequence some of the needs that were originally envisioned for that building have changed.

Our current thinking is pretty much as follows, Mr. Conte. I know you have a very strong interest in this. Rather than put the building off on a far corner of the campus, we are now considering moving the site of that building much closer to the center of campus where it will be more closely aligned with other buildings where other scientists focusing on the neurosciences will be conducting their research.

The original building also called for a major primate facility. We are considering expanding that part of the design of the building so it will provide a primate facility for not just NICHD but also for the neuroscientists from the National Institute of Mental Health and National Institute of Neurological and Communicative Disorders and Stroke who do comparable research.

By putting those programs together with our intramural scientists in the neurosciences area, we can foster the collaborative interaction among those programs and have a more economical operation as well. So we are currently reconceptualizing that building.

It will still be a NICHD building. It will put together our intramural program for the benefit of those scientists, but can also serve the purpose of providing a primate research facility for our work and the work of two other institutes as well as bring together much of the neurosciences research on the campus.

The reason that that contract has not been let for the redesign has been our work in reconceptualizing this building.

Mr. CONTE. I hope you put this on the front burner and get moving on it. I am not getting any younger. I want to see it done before I leave here.

LEADING CAUSES OF INFANT DEATH

Doctor, I notice an interesting divergence in your statements. In your prepared statement you indicate the sudden infant death syndrome is a leading cause of death once infants pass the critical newborn period to one year, and in your justifications, on page 84, it states that mental and physical defects resulting from faulty development remain the leading cause of death under one year of age. Not to quibble, I was wondering how you square those two statements.

Are there any developments to report on sudden infant death syndrome? Those figures I assume relate to the United States, of course.

I would assume that for the world as a whole infectious diseases probably would be the leading cause of death. Is that fair?

Dr. ALEXANDER. Yes, sir. Let me try to clarify those statements. They are not incompatible, but I apologize for the lack of clarity. If you look at infant mortality, which is all deaths under one year of age, birth defects or congenital anomalies are the leading cause.

They presently account for about 22 percent of infant deaths. The majority of those deaths occur in the first month of life. Sudden Infant Death Syndrome is rare during the first month of life.

After the first month of life, Sudden Infant Death Syndrome, rather than congenital anomalies, becomes the leading cause of infant mortality.

Overall, about 22 percent of infant deaths are due to congenital anomalies and about 13 percent to Sudden Infant Death Syndrome. Respiratory Distress Syndrome and a few other causes are next.

The number of SIDS deaths is presently tabulated around 5300 a year. It is the leading cause between a month and a year, but not the leading cause overall.

Mr. CONTE. I see. That is a good explanation.

Mr. Chairman, I have some other questions and I will submit them for the record so Dr. Alexander can answer them at his leisure.

Mr. NATCHER. Mr. Stokes.

BLACK TEENAGE PREGNANCY

Mr. STOKES. Thank you, Mr. Chairman.

Dr. Alexander, I noticed in your statement that you said a large proportion of the nation's unintended pregnancies occur among teenagers. Recently, there have been several articles written about this subject in national publications. Also, Bill Moyers appeared in a television documentary about teenage pregnancies and births among black teenage females.

Have you had a chance to study this tremendous problem?

Dr. ALEXANDER. We have been active in the teenage pregnancy area for a number of years, Mr. Stokes. Much of the data Mr. Moyers and others have used has been gathered by investigators that we have supported.

RACIAL VARIANCES IN TEENAGE PREGNANCY

Mr. STOKES. What are the differences between black female teenagers having children and white female teenagers having children?

Dr. ALEXANDER. In terms of number or outcome?

Mr. STOKES. Number, outcome, the entire picture.

Dr. ALEXANDER. In terms of numbers, if you look at just births under age 15, blacks constitute about 12 percent of the population, but the majority of births under age 15 are to blacks, about 5,000 versus 4,000. This is a small number overall.

About 29 percent of births to women age 15 to 19 are to blacks, again, with their constituting about 12 percent of the population. So the black teenager is more likely than the white teenager to have a pregnancy.

Mr. HOYER. Would you repeat that?

Dr. ALEXANDER. There are about 5,400 births to blacks, and 4,000 births to whites under the age of 15.

Between ages 15 to 19, about 29 percent of the births are to blacks.

Mr. STOKES. What total are we talking about?

Dr. ALEXANDER. Total numbers, I will have to supply those for the record, Mr. Stokes.

[The information follows:]

TEENAGE PREGNANCY

In 1983, the last year for which we have data, there were 499,038 babies born to women under the age of 20. For teens under age 15 there were 9,752 births. The distribution by race was:

Black	5,439
White	4,031
Other races	282
Total	9,752

Among women aged 15-19, there were 489,286 births. The distribution by race was:

Black	136,666
White	338,152
Other races	14,468
Total	489,286

TEENAGE PREGNANCY

Mr. **Hoyer**. Excuse me, Mr. Stokes.

Mr. **Stokes**. That is quite all right.

Dr. **Alexander**. We do know a number of things. The black teenager is more likely to initiate sexual activity at an earlier age by one to two years. However, their contraceptive use is approximately the same as the white teenager. The black teenager is less likely to resolve a first pregnancy by abortion than a white teenager.

They run an almost equal likelihood of not completing school. The black family actually in some ways tends to do better in outcome. There seems to be a better, stronger family support network for the black teenager with a pregnancy than for the white, but the likelihood of going back to school is not good for either.

Mr. **Stokes**. Have you looked at this over a period of several years to see whether in either category; that is, the white teenage category or the black teenage category, there is either an increase or a decrease in the number of children born out of wedlock?

Dr. **Alexander**. The number of out-of-wedlock births has been increasing.

Mr. **Stokes**. For both categories?

Dr. **Alexander**. For both. The specific figures on that, Mr. Stokes, I will have to supply for the record.

The total number of births to unmarried women age 15 to 19 years is about 261,000. About 132,000 of these are to white, and 120,000 to black teenagers. This is in 1983.

To give you a change over the years, I will have to supply that for the record.

Mr. **Stokes**. I would like for you to feel free to expand on this matter in the record for me.

Dr. **Alexander**. I will be pleased to do that.

[The information follows:]

TREND IN OUT-OF-WEDLOCK BIRTHS

From 1960 to 1983, the number of babies born to unmarried teenagers almost tripled (92,000 to 270,000). The rate at which unmarried teenagers bear children increased from 15.3 birhts per 1,000 to 29.7. A greater percentage of the teen mothers are 18 or 19 nowadays, but the absolute number of unmarried mothers has grown at the younger ages.

NUMBER OF BIRTHS TO UNMARRIED WOMEN UNDER AGE 20

Ages	1960	1970	1983
Under 15	4,600	9,500	8,816
15-17	43,700	96,000	116,625
18-19	43,400	94,300	144,635
Total	91,700	199,800	270,076

There are more out-of-wedlock births among black teens at the youngest ages (under 15)—5,354 versus 3,222 for whites—and roughly equivalent numbers of out-of-wedlock births at ages 15-19—120,926 for black teens and 132,494 for white teens. The rates are higher for blacks, 86.4 births per 1,000 unmarried black teens aged 15-19 versus 18.5 births per 1,000 unmarried whites. However, white rates have been increasing, and black rates have been declining.

OUT-OF-WEDLOCK BIRTH RATE [1] FOR TEENS, 1970, 1983

Ages	1970	1983
White rate:		
15-17	7.5	13.5
18-19	17.6	26.1
Black rate:		
15-17	77.9	67.1
18-19	136.4	114.0

[1] Births to unmarried women per 1,000 unmarried women.

CHILDREN BORN OUT OF WEDLOCK

Mr. STOKES. Is it a fact that two-thirds of the children born out of wedlock in the country are actually born to adult women 20 years of age and above?

Dr. ALEXANDER. Yes, that is correct. It is at least two-thirds.

RESEARCH GRANTS TO HISTORICALLY BLACK COLLEGES

Mr. STOKES. In 1984, NICHD awarded only $281,590 in research grants to historically black colleges. Can you tell us what you are doing to increase your institute's level of support to these historically black colleges?

Dr. ALEXANDER. This is really being done as part of an overall NIH effort among the historically black colleges and universities. The Institute has a program in which our intramural scientists go on mini-sabbaticals to teach for a period of time in some of these minority institutions.

We have a program of what we call extramural associates. Many of these associates come in from the historically black colleges and universities to gain experience within the NIH system. They go back to their own institutions knowing how the NIH system works and are better able to assist their faculty in grant applications and their students in fellowship applications.

The efforts that we are making have really been part of the NIH overall effort rather than specific institute efforts.

NICHD MINORITY PROGRAMS

Mr. **Stokes**. Do you establish goals for your senior administrators for addressing minority program and personnel issues?

Dr. **Alexander**. Every senior administrator has, as part of their annual performance plan, adherence to equal employment opportunity goals and policies and programs.

They are evaluated on that aspect of their performance equally with other aspects.

Mr. **Stokes**. I would appreciate it if you would supply for the record the following information for SES positions, senior level administrator, senior level professional: the current number of all positions and the current number of these positions currently occupied by blacks and/or minorities.

[The information follows:]

MINORITIES IN SENIOR NICHD POSITIONS

	SES	Senior level administrator	Senior level professional
Non-minorities	7	19	55
Blacks	0	2	5
Other minorities	0	0	8
Total	7	21	68

Dr. **Alexander**. We will do that, sir.

Mr. **Stokes**. Thank you very much, Dr. Alexander.

Thank you, Mr. Chairman.

Mr. **Natcher**. Mr. Hoyer.

USE OF CONTRACEPTIVES

Mr. **Hoyer**. Thank you very much, Mr. Chairman.

I was going to also ask you about the items you deal with at page 6 of your statement regarding teenage pregnancy. Obviously it is an issue that has received lots of attention as Congressman Stokes has pointed out and one which a lot of us think is very important.

You imply and refer to several institute-supported studies that have examined factors differentiating sexual activities between those who actively use contraceptives from those who do not. Pursuant to those studies have you made any recommendations as to how the issue might be addressed on a national coordinated basis?

Dr. **Alexander**. Mr. Hoyer, the results of those studies indicate a number of factors about effective use of contraception. The teenager who is more likely to be an effective user of contraception is likely to be older, to be involved in an ongoing relationship rather than multiple relationships, and to have characteristics of a personal problem solver who is successful in a number of areas rather than just in contraception. Access to services also has emerged as a particularly important factor.

INFORMATION ON FAMILY PLANNING

Mr. **Hoyer**. Doctor, let me stop you on access to services. I would presume that to be the case, but what do you specifically mean as it relates to education, public health services, counseling services? What specifically do you have in mind?

Dr. **Alexander**. Access to information basically on the whole reproductive process, by which I mean sex education, and access to family planning information on a confidential basis. One thing that has been particularly effective has been school based clinics.

The Ramsey-St. Paul system is one example that is often cited as a particularly outstanding operation where in school based clinics, information on family planning is provided as part of other health care services for teenagers.

Mr. **Hoyer**. When you say provided on a confidential basis, I presume you mean provided to the client or the teenager on a basis that would not—that the teenager would understand, would not be discussed with others including the parents?

Dr. **Alexander**. That is one thing that has emerged from the research.

Mr. **Hoyer**. And that if the teenager feels that the parent will be privy to the information is that a substantial or minimal deterrence to the teenager seeking counseling?

Dr. **Alexander**. I am not sure I have data to indicate whether it is substantial or minimal. It does serve as some degree of deterrent. I can't quantify it.

Mr. **Hoyer**. What is happening with your recommendations? Do you know? Doctor, specifically, what I want to know is does that go to NIH? Does NIH make that departmental policy?

Is the Department trying to reach some of the folks in the Administration?

Dr. **Alexander**. We really have not made specific recommendations. The results of these studies have been published.

They have been used by various groups as they have attempted to set up programs and have been applied in that way.

COORDINATION WITH DR. NICKENS

Mr. **Hoyer**. How closely do you work with Dr. Nickens?

Dr. **Alexander**. Dr. Nickens has just been appointed on the Secretary's staff to address minority concerns.

Mr. **Hoyer**. I know that.

Dr. **Alexander**. Dr. Nickens was a member of the Subcommittee on Infant Mortality and Low Birth Weight of the Black and Minority Health Task Force that was chaired by Dr. Wendy Baldwin of our Institute staff.

So he has been involved with our staff very closely in this whole area of infant mortality and low birth weight. We plan to continue that close relationship as he assumes his new role. I have a meeting set up already with him and Dr. Baldwin to discuss activities that we might jointly undertake.

LOW BIRTH WEIGHT AND AGE OF THE MOTHER

Mr. **Hoyer**. As I understand it low birth weight, which you indicate is the principal problem, is related to the age of the mother in many instances, is that correct?

Dr. **Alexander**. Yes, at the extremes of child bearing. The woman under age 15 has about a 14 percent risk of a low birth weight baby. Age 15 to 19, it is about nine percent. Then it drops below 7 percent and doesn't rise again until after age 39.

OPENING STATEMENT PREPARATION

Mr. HOYER. Doctor, this question does not relate, per se, to your expertise. How are these statements prepared? I know that all of these statements are prepared pretty much with the same format.

My perception of these statements is they are excellent, very interesting and I like them. This is a seven-page statement, two lines of however many lines deal with the budget, deal with appropriations. How do these statements get made up?

Dr. ALEXANDER. We have very specific guidelines in terms of format and length of statements.

Mr. HOYER. Who establishes those formats, Mr. Miller or somebody at NIH? Does OMB give directions?

Dr. ALEXANDER. Mr. Williams?

Mr. WILLIAMS. These are done internally. I am not sure myself I can describe how they are done in the public health service, but the Office of Management and Budget is not involved in the formatting of these statements.

Mr. HOYER. They are all uniform and that is good. At least you can understand where they are coming from.

Dr. ALEXANDER. We format them according to directions from the NIH. We try to emphasize in those statements interesting and exciting areas of science that are of public health concern. They are really designed to accompany the much longer and formal budget document that is submitted separately and is not nearly as exciting reading sometimes.

ORIGINAL FY 1987 NICHD BUDGET REQUEST

Mr. HOYER. The others are not nearly as exciting. You are absolutely right on that. I am sure my time must have expired so I will yield back to the Chairman.

Just one more question, Mr. Chairman.

What was your original request to NIH?

Dr. ALEXANDER. The request to the NIH was $374,148,000.

Mr. HOYER. What won't you be able to do as a result of that request not being approved and being cut by $65 million?

Dr. ALEXANDER. This will impact primarily on the number of grants we are able to fund. It will have an impact on the support we are providing to our centers, on the number of new contract activities that we can initiate, on both the low birth weight prevention and contraceptive development initiatives and on the amount of training we can support.

EFFECT OF REDUCTIONS

Mr. HOYER. Doctor, because I can't digest that right away, what does that mean? What grants are going to suffer? What health needs or what health concerns in the country and of our population are we not going to respond to that you had planned to respond to with that extra $65 million or approximately 25 percent, 20 percent?

Dr. **Alexander**. The requested amount would have provided funds for substantial expansion of the low birth weight prevention initiative and the contraceptive development initiative. It would also have provided——

Mr. **Hoyer**. How much for the contraceptive initiative?

Dr. **Alexander**. $11.7 million.

Mr. **Hoyer**. Without that $11.7 million how much do you have left for that initiative?

Dr. **Alexander**. Approximately 11 million.

Mr. **Hoyer**. So you wanted to double it?

Dr. **Alexander**. Yes.

Mr. **Hoyer**. A little more than double. All right, sir. What was next?

Dr. **Alexander**. We had planned to initiate use of our mental retardation research centers for the conduct of clinical trials in a network comparable to what we are doing with the neonatal intensive care units evaluation network. These are a pre-existing network but they never have functioned effectively to interact for the conduct of clinical trials.

We will not be able to undertake that initiative.

Mr. **Hoyer**. How much was dedicated to that objective?

Dr. **Alexander**. Approximately $2.7 million.

Mr. **Hoyer**. I didn't ask you on the first of the three that we mentioned so far. I add up about 13. What was the expansion?

Dr. **Alexander**. The low birth weight prevention initiative was 11 million.

Mr. **Hoyer**. Okay. We have got 40 to go. I am not trying to be difficult. The frustration I have on these presentations and the reason I bring it up in terms of the statement, is that this committee is called upon to make policy. You, as the expert, albeit not at the high policy level, are the expert that we rely on to tell us what are the health needs of the United States that we can respond to with X number of dollars. One of the frustrations of the statements is understandably because policy makers have made key decisions and it is not your role to carp at or second guess the policy makers in a democratic way.

I understand that. However, it is ours. That is how the system works, and therefore, I want to get at what is the cost of not appropriating that $65 million. I realize we are in a tight fiscal situation and we may not be able to respond, but I would like to know what we are not responding to.

So if you could quickly give me the balance of $40 million.

Dr. **Alexander**. The clinical trial for the pertussis vaccine proposed for——

Mr. **Hoyer**. Are these all relatively small? Let me be more specific because the chairman will lose patience with me and rightfully so.

There are two $11 million items. Are there any other significantly large—and when I say "significantly large", ten million or above items?

Dr. **Alexander**. The pertussis clinical trial in the United States, I mentioned, will have to be deferred. It is about $2.7 million.

Mr. **Hoyer**. I imagine there are a number of those but do we have any—I find for instance the contraceptive and the low birth weight $11 million cuts very significant. Are there others in that category that are a particular concern to you, Doctor?

How is that for making it even tougher?

Dr. ALEXANDER. Mr. Hoyer, we also would have a shortfall of $6 million in our research centers and a shortfall in the research project grants accounting for most of the rest of the difference.

RETT SYNDROME

Mr. HOYER. Last question, and this is really more of a comment. I want to congratulate you and thank you. I know you in concert with Dr. Goldstein participated in the Rett Syndrome Conference that was undertaken at Johns Hopkins. Dr. Goldstein has testified he felt that that was a very, very successful conference, more successful than had been anticipated and more significant than had been anticipated.

I would like you if you could, Doctor, having thanked you, if you could briefly give me your views and comments on that conference on Rett Syndrome.

Dr. ALEXANDER. I will be glad to do that, Mr. Hoyer.

I attended most of that conference. I found that as Dr. Goldstein did, a conference that exceeded expectations. Dr. Moser succeeded in attracting to that conference virtually every leading researcher in the world who is involved with research on Rett Syndrome.

It served both as a conference that permitted sharing of the most up-to-date information on the latest research findings related to Rett Syndrome as well as a catalyst for investigators to go back and undertake additional studies that they had not thought of until they had the chance for interaction with their colleagues.

We also used it as an opportunity to encourage investigators at that conference to submit research grant applications for studies on Rett Syndrome. We know that we will be receiving at least one June 1st that we hope will be of outstanding quality and that we will be able to fund it.

Mr. HOYER. Thank you very much. Again, I want to thank you for the attention that you and Dr. Goldstein and others within NIH have given to this particular area.

It may be small, but it is I think a significant one. Mr. Chairman, again, thank you for giving me the time you have allotted me. Thank you, sir.

Mr. NATCHER. Dr. Alexander, I want to thank you and your associates for appearing before the committee at this time in behalf of your budget request for the fiscal year 1987. It has been a good hearing. We appreciate it.

Dr. ALEXANDER. Thank you, Mr. Chairman.

[The following questions were submitted to be answered for the record:]

PERTUSSIS VACCINE

Mr. Conte. With regard to pertussis, where the potential side effects of the existing vaccine have caused so much controversy, you state that a new vaccine developed at NICHD is about to go into trial in Sweden. How is this vaccine superior to the existing one?

Dr. Alexander. The new vaccine is based upon a single component of the pertussis organism, pertussis toxin. Interestingly, while this is the component that causes the symptoms of whooping cough, it also appears to induce immunity to the infection. The inactivated, highly purified toxin should produce many fewer side effects than the existing vaccine which is an impure, poorly standardized mixture of many pertussis components--most of which seem to be unnecessary for an effective vaccine. Moreover, the structure of a single pure component can be analyzed and controlled by the very latest chemical and physical techniques, insuring that our vaccine will remain absolutely stable, predictable and safe.

Mr. Conte. What would you think is the time line for the approval and availability of this vaccine, if it turns out to be superior to the existing one?

Dr. Alexander. It will require about three years of extensive clinical trials before we have sufficient information to insure an entirely safe and effective vaccine, followed by FDA approval and commercial production. Just to prove efficacy would require very little time, but since the most serious side effects of the existing pertussis vaccine are rare, we will have to give the new vaccine to many thousands of children before we can be sure that the rare incidence of serious side effects has been significantly reduced.

Mr. Conte. From time to time, we hear that there is a new pertussis vaccine coming out of Japan and that is cited as to how far biomedical research in Japan has come, to the point where it is challenging, if not overtaking the state of research in the U.S. Would you comment on that?

Dr. Alexander. The new pertussis vaccine developed in Japan, while probably an improvement on the existing pertussis vaccine, is not based upon a highly purified and rigorously standardized single component. Rather, it is still a mixture of pertussis components, fewer than in the existing vaccine, but difficult to standardize. While the Japanese vaccine has been given to millions of children, the results will be difficult to interpret because of the problem of standardizing this vaccine and also because the trial in Japan has, in our view, not been adequately controlled. Nevertheless, the Japanese have contributed greatly to pertussis research, showing, for example, that monoclonal antibody to the toxin protects animals from the infection.

LEARNING DISABILITIES

Mr. Conte. Would you tell us a little about the work you are doing in the area of learning disabilities?

Dr. Alexander. The largest part of this research has as its goal the development of basic knowledge concerning the biobehavioral mechanisms that are necessary for learning across the developmental span from birth to the onset of adulthood. In general the research is designed to answer questions about normal learning processes at different developmental stages. However, a significant portion of it also directly addresses learning disabilities. Thus a major focus of our program is upon dyslexia, i.e., the inability to acquire reading. Research on this topic is investigating brain/behavior links in the reading process; the potential for genetic factors to be in part responsible for the disability; and linguistic factors that may be relevant to unraveling the puzzle of this significant behavioral disorder. In addition to dyslexia, the program also supports research on learning deficits such as attention deficit disorders, hyperactivity, and other behavioral processes involved in delayed learning. Such work involves studies of cognitive development and behavioral and biological mechanisms of memory and information processing in children. Much of this research provides the basis for developing assessment techniques for physicians and other health care providers to screen infants and detect learning deficits early in life. The principles and mechanisms discovered are also employed by scientists and physicians to develop remediation procedures to help those identified as having deficits to live a more normal life. For example, several of our grantees in our Small Business Innovation Research program are developing computerized systems for diagnosis and remediation of dyslexia and other learning disabilities.

ACCIDENT PREVENTION

Mr. Conte. Last year, in view of the fact that accidents are the leading cause of death in children, once infancy is past, you indicated that you would start a program of accident prevention. In this year's statement, you indicate that you are beginning to make awards for grants in this area. What types of research are you funding here, and what kind of an impact do you think that this research can have on the accident rate for children?

Dr. Alexander. The NICHD is expanding its support of research on childhood injury to develop basic knowledge concerning factors that may either predict or help prevent injury. These efforts rely primarily on the behavioral sciences.

For example, one approach taken by behavioral scientists has been to employ behavioral principles to develop parent training techniques that influence them to safety proof their homes. One such grantee is Dr. Edward Christophersen at the University of Kansas. He developed a behavioral counselling program in a well-child clinic to encourage parents to lower the water temperature setting of their hot water heaters and thereby to prevent scald burns. The effectiveness of the counselling was monitored by checking hot water temperature with an electronic thermometer in the homes of the participating parents. Sixty-five percent of the counselled parents had the correct setting while none of the parents in the control group did. In other research that has just gotten under way, Dr. Michael [illegible] of the Johns Hopkins University is studying the behavioral characteristics of young children in such hazardous environments. His experiments employ situations that simulate reality with flashing paint-like substance under two conditions: group play with an enriched environment of toys appropriate to the age of the child, and an impoverished setting where no toys were available, only clothespins, plastic container lids and socks. The preliminary findings indicated that the total mouthing (pica) of the mock paint-like substance was from four to nine times more frequent in the impoverished environment than the group play or enriched environment. While it might have been predicted that the children given more toys would spend more time playing with them, the important observation was that the ingestion of the mock hazard flakes virtually disappeared. Such results suggest that environmental enrichment for young children might be an effective supplement or alternative to the extremely expensive practice of "deleading" a house.

We also have plans to fund research that will attempt to ascertain how behavioral characteristics of children and their families interact with aspects of the home environment to predict the likelihood of childhood injuries. Such research would involve the use of a prospective longitudinal design in which children would be followed over a period of years to determine the validity of the predictive factors.

Research studies such as those described above should provide a scientific basis for isolating risk factors that are predictable antecedents of accidents, lead to the development of intervention strategies for preventing childhood injuries, and provide information for pediatricians and public health officials to educate parents and children concerning this major public health problem.

Another aspect of our initiative in this area is the recognition of the need for improved knowledge concerning appropriate methods required for research on childhood injuries and their prevention. To accomplish this objective, the NICHD with input from the American Academy of Pediatrics, the American Psychological Association, and the Society for Research in Child Development, is organizing a research workshop on this topic and will make the results available to investigators in this field to assist them in planning and designing studies of childhood injury.

CONTRACEPTIVE DEVELOPMENT INITIATIVE

Mr. Conte. You have mentioned in the past the Institute's contraceptive development initiative. Please outline the major features and specific outcomes or products of the initiative.

Dr. Alexander. The major features of the contraceptive development initiative involve research in four areas: (1) basic research on human reproduction which can identify new fertility regulation approaches; (2) applied research in contraceptive development; (3) assessment of safety and efficacy of existing methods of contraception; and (4) research on the behavioral aspects of contraceptive use.

The goals of the basic research component are to provide leads for the development of a new generation of modalities for fertility regulation through research on the following topics: Immunology related to contraception; the prevention of gamete maturation; the discovery of new substances in the body that may have contraceptive potential; blockade of the action of the primary fertility hormones in the body; identification of steps in reproductive processes that are vulnerable to interdiction; and the application and introduction of new and highly sophisticated technologies into research related to contraception.

In the applied area of contraceptive development, the Institute is currently supporting several clinical trials involving new drugs and devices that may prove to be attractive to various segments of the population. At the laboratory level we are pursuing synthesis and testing of new drugs, development of new barrier methods, development of new methods of drug administration, and the development of antifertility vaccines.

Research on the safety and efficacy of existing contraceptive methods would include studies of methods used in foreign countries but not approved for use in the United States; modifications of IUD's that may make them safer; and studies of the effects of recent formulations of oral contraceptives on various aspects of women's health, including the risk of cardiovascular disease, cancer, and indicators of overall mental and physical health.

Research in the demographic and behavioral sciences would include studies of factors tending to encourage or discourage the use of various methods of fertility control. These would include studies of the acceptability and probable utilization of proposed new methods; the choice, effectiveness, and continuation of use of existing methods; and the strength of motivation for preventing pregnancy.

ISOLATION OF INHIBIN

Mr. Conte. Tell us a little about the natural hormone you have isolated called "inhibin" and who is involved in this development effort.

Dr. Alexander. Inhibin is a natural hormone that appears to function as a highly specific inhibitor of the secretion of follicle stimulating hormone (FSH). FSH is often referred to as one of the two "fertility" hormones secreted by the pituitary gland because it is required for the promotion of ovulation in women and sperm production in men. The recent determination of the structure of inhibin paves the way for the design of new contraceptives for both men and women based on the inhibition of FSH secretion. Because it occurs naturally in the body and is highly specific in its site of action, inhibin (or analogs of it) may regulate fertility without eliciting undesirable side effects in other parts of the body. Dr. Roger Guillemin and his colleagues at the Salk Institute in San Diego, along with other colleagues at Genentech, also in California, were the first to determine the structure of inhibin.

POTENTIAL USES OF RU 486

Mr. Conte. There has been some controversy over a substance called RU-486. Tell us about the potential uses of this drug and what aspects of the use of the drug the Institute is studying.

Dr. Alexander. The drug RU 486 was developed in France approximately six years ago. It has two types of actions. First, it is an antiglucocorticoid (blocks effects of cortisone and related hormones). This action makes it useful for physiologic studies, because it can block glucocorticoid activity to help us understand the normal role of glucocorticoids in the body. It has also already had diagnostic and therapeutic applications at the NIH, with spectacular success in treating patients with Cushing's syndrome, a disease caused by excess glucocorticoid (cortisone) production by the body. This action is also being studied for potential use in treating glaucoma and decreasing immune system suppression in Acquired Immune Deficiency Syndrome (AIDS).

Second, RU 486 has an antiprogesterone action. Investigators at the NIH and elsewhere are using this property of the drug to study the normal role of progesterone in reproductive function, as well as its potential use as a contraceptive and as a treatment for some reproductive disorders such as endometriosis. Because of its antiprogesterone action, another extremely important potential use of RU 486 that is being studied by NIH is in treatment of breast cancer. A major recent advance in breast cancer chemotherapy has been the use of an estrogen blocking drug, Tamoxifen, in tumors that are estrogen responsive. RU 486 now provides a potential chemotherapeutic drug for other breast cancers that are progesterone responsive, and this possibility for use as a progesterone blocking drug is being pursued in cancer research.

Some investigators are conducting research on use of RU 486 to induce abortion. The research that is being done on RU 486 as a potential abortifacient is not being supported by the NIH.

There are many other potential applications for RU 486. These include developing ways to overcome discomfort and infertility resulting from polycystic ovarian disease and endometriosis; treatment of other progesterone sensitive cancers, such as ovarian, endometrial, and prostate cancer; and alleviation of symptoms in premenstrual syndrome and fibrocystic disease of the breast.

MENTAL RETARDATION RESEARCH CENTERS

Mr. Conte. For how many years now has the Institute funded a program of Mental Retardation Research Centers?

Dr. Alexander. NICHD has been funding Mental Retardation Research Centers for 20 years.

Mr. Conte. Have the same centers been funded throughout the history of the program?

Dr. Alexander. Eleven of the twelve Mental Retardation Research Centers currently being supported have been funded throughout the history of the program. A center at the University of California, San Francisco, was added in 1982, the same year a center was dropped at the University of Cincinnati.

Mr. Conte. Has this investment in these research centers been worthwhile?

Dr. Alexander. Yes, the Mental Retardation Research Centers (MRRCs) have been highly worthwhile. The concept underlying the establishment of the Centers was to facilitate the development of new research intiatives on the causes and methods for prevention and treatment of mental retardation. As was expected when construction grants were given to the initial 12 Centers, one of the major ways to reach this goal has proven to be interdisciplinary research that fosters innovative breakthroughs in finding solutions to the causes of mental retardation. Another advantage that was foreseen, and subsequently shown, in the MRRCs was efficiency derived from sharing resources and facilities provided by the Center core grants from the NICHD. At the same time, investigators sharing resources have also shared research techniques and ideas, and this invariably leads to innovative findings.

The future of research in any area is shaped by the young scientists being trained for work in that area. The MRRCs were intended as training sites to attract young scientists to careers in research on mental retardation. The result of this effort has been the flow of investigators trained in the Centers who are now working in other institutions around the country as the new leaders in mental retardation research.

The MRRCs have also provided a network of investigators who are prepared to undertake new solutions related to mental retardation, such as the recently planned collaborative clinical trials on methods of prevention and treatment. The Centers have been the centerpiece of the NICHD program in mental retardation research, receiving more than 50% of the Institute's grant funds in mental retardation.

Mr. Conte. What kinds of return on that investment would you say we have received?

Dr. Alexander. The MRRCs have expanded the knowledge base of science applied to problems of mental retardation. They have identified new causes of mental retardation and thereby have reduced the percentage of mental retardation due to unknown causes. In addition, research in the Centers has contributed to the prevention of some kinds of mental retardation and to the treatment of other kinds of mental retardation and accompanying conditions. In all of the Centers there are many examples of interdisciplinary research which have led to prevention or treatment of mental retardation. A number of examples of these follow:

- Discovery of Fragile-X Syndrome, a new genetic cause of mental retardation
- Description of Fetal Alcohol Syndrome
- Treatment of self-injurious behavior in persons with severe and profound mental retardation
- Prevention of mild mental retardation through early educational day care

- Behavioral training of persons with mental retardation to live in community settings
- Development of screening for metabolic diseases which cause mental retardation

We are on the frontier of many new and exciting research areas that will contribute to the treatment and prevention of known and yet unknown causes of mental retardation. We expect that the Mental Retardation Research Centers will provide many of these future research findings and contribute to further reduction in mental retardation.

CLINICAL TRIALS

Mr. Conte. Are there any clinical trials under way that will be curtailed either by the revised FY 1986 proposed budget, or the FY 1987 budget proposal?

Dr. Alexander. There are eight major clinical trials whose initial awards will be reduced under the proposed budget in FY 1986 and which will also receive reduced awards in FY 1987.

1) The network of maternal-fetal medicine research units and 2) the network of neonatal intensive care research units will receive only enough funding to provide for protocol development in FY 1986. These networks will initiate clinical trials in FY 1987, although at a lower level than originally planned.

3) Parenteral amino acid requirement in low birth weight infants who cannot be fed by the mouth during the first one or two weeks of life;

4) Capronor implantable drug delivery system for the contraceptive drug levonorgestrel;

5) New drug therapy in treatment of nephropathic cystinosis, a genetic disease characterized by poor body growth and end-stage renal disease;

6) Efficacy of routine ultrasound screening in pregnancy to aid in diagnosis of twin pregnancy, accurate gestational age, and congenital anomalies;

7) Effectiveness of physical therapy for infants at risk for developmental disabilities and mental retardation;

8) Field trials in Sweden of the pertussis vaccine developed by NICHD intramural scientists.

Mr. Conte. Are there any clinical trials ready to go that you will not be able to undertake due to budget constraints in FY 1986 or FY 1987?

Dr. Alexander. In FY 1986 the clinical trials planned for the networks of maternal-fetal medicine units and the neonatal intensive care units will not be undertaken.

In FY 1987, these clinical trials will be delayed:

1) Effects of synthetic growth hormone releasing factors on growth hormone deficient patients;
2) Nutrition and other factors relating to pregnancy and poor pregnancy outcome among lower socioeconomic status inner city minority populations;
3) Factors influencing breast feeding to improve the incidence and duration of breast feeding;
4) Mental Retardation Research Centers network for collaborative clinical trials in the prevention and amelioration of mental retardation;
5) Clinical trials of pertussis vaccine in the United States;
6) Clinical trials of Hemophilus influenzae vaccine to prevent meningitis and subsequent mental retardation in infants and young children;
7) Clinical studies with a long-acting spermicidal formulation;
8) Certain clinical trials within the network of maternal/fetal medicine units;
9) Certain clinical trials within the network of neonatal intensive care units.

CLINICAL TRIALS

Mr. Conte. For the record, please provide a list of clinical trials under way.

Dr. Alexander. The following list indicates major ongoing clinical trials of the NICHD.

° Prevention of Cytomegalovirus (CMV) Disease

° Effects of Maternal PKU on Pregnancy Outcome

° Prematurity and Gestational Genitourinary Infections

° Intervention to Reduce Smoking During Pregnancy

° Effects of Tonsil-Adenoid Surgery on Throat Infection

° Extracorporeal Membrane Oxygenation (ECMO) in Newborn Respiratory Failure

° Strict Control of Diabetes in Pregnancy

° Clinical Studies on Human Milk

° Spermicides and Sexually Transmitted Diseases

° Phase II Clinical Studies with LHRH Agonists

- Human Biochemical Genetics
- Growth Hormone Releasing Factors
- Physiology of Puberty
- Mechanism of Pubertal Growth
- Protein Requirements of Infants and Children
- Iron Deficiency Anemia and Infant Behavior
- Perinatal Effects of Support During Labor
- Treatment Evaluation in Premenstrual Syndrome Patients
- Surfactant Biochemical Development and Stabilization
- Comparison of Chorion Villus Sampling and Amniocentesis
- Clinical Pharmacology of LHRH Antagonists
- L-Carnitine Treatment of Chronic Kidney Disease
- Development and Testing of Improved Spermicidal Contraceptives
- Prevention of Intrauterine Growth Retardation by Bed Rest
- Evaluation of a Polyvinyl Vaginal Contraceptive Sponge
- The Effect of Parent Weight on Obese Young Children
- Treatment of Obesity in Children and Adolescents
- Calcium and Phosphorus Nutrition in High Risk Infants
- Prevention of Otitis Media in Infants
- Treatment of Precocious Puberty and Other Endocrine Disorders with Leutinizing Hormone-Releasing Hormone
- Treatment of Infertility with Gonadotropin-Releasing Hormone in Men and Women.
- Effects of Growth Hormone Therapy on Children with Extreme Short Stature
- Intervention Strategies in Gestational Diabetes Mellitus

The following is a list of major new clinical trials in FY 1986.

- Parenteral Amino Acid Requirements in Low Birth Weight Infants
- Clinical Studies with Capronor Implantable Drug Delivery System

- Clinical Trial of New Drug Therapy in Treatment of Nephropathic Cystinosis
- Efficacy of Routine Ultrasound Screening in Pregnancy
- Effectiveness of Physical Therapy for Infants at Risk for Developmental Disabilities and Mental Retardation
- Pertussis Trials in Sweden

FY 1986 RESCISSION

Mr. Early. How was the amount of the rescission for your institute arrived at?

Dr. Alexander. While the OMB directed that the total amount of the FY 1986 rescission be taken from research project grants, the Director, NIH, had responsibility for allocating specific rescission amounts to each Institute. The amount of each Institute's rescission was determined in two steps--a simple proration of the total rescission against each Institute's funding for research project grants, and then further adjustments to reflect NIH research priorities.

Mr. Early. How did you decide what program areas you would apply the rescission to?

Dr. Alexander. The rescission was applied to research project grants across the board. No particular program area was affected more than another.

Mr. Early. Doctor, in your professional judgment, overall what kind of an impact would this rescission ($1.150 million) in addition to the $13.838 million sequestered, have on your programs in FY86?

Dr. Alexander. The rescission would result in the funding of 16 fewer research project grants, with the reduction applied across the board by program area.

REDUCTIONS IN GRANTS

Mr. Early. According to the budget justification there will be downward negotiations of 9.8% and 9.6% in competing and non-competing grants, respectively. Will each grant be reduced by these amounts?

Dr. Alexander. No. These figures represent the reduction in the average amount of all grants, but each grant will not necessarily be reduced by the same amount.

Mr. Early. What impact will reductions of this size have on the Institute's research activities?

Dr. Alexander. We expect that grant supported investigators will be able to continue their research, but at moderately reduced pace and scope.

Mr. Early. In your professional judgment, Doctor, do you have any serious concerns about the size of the downward negotiations the project grants are being forced to take under this budget request? Historically, these reductions have averaged 3% for competing grants and 1% for noncompeting grants.

Dr. Alexander. Yes, while I agree some reduction from recommended levels can be accomplished with minimal effect, I am seriously concerned that reductions of this size will reduce the funds available to individual investigators about as far as we can go without damage to the essence of what the grantees have proposed to accomplish. In other words, the investigators can continue to do their work, albeit at a slower pace or change in direction of their work, in order to effect the necessary savings.

Mr. Early. The budget indicates that direct costs for research centers will be reduced by 12% in FY86 and 16% in FY87. Are reductions of this size something we need to be concerned about?

Dr. Alexander. Yes, we are concerned. The comparable reduction in 1984 and 1985 was 4%. However, this kind of reduction is preferable to reducing the number of centers that receive support at all.

RESEARCH CENTERS

Mr. Early. What effect will these cuts have on the research programs at these centers?

Dr. Alexander. NICHD has just begun a concentrated effort to initiate collaborative studies among the Mental Retardation Research Centers on topics which are difficult to study by any one group of scientists. One example is a clinical trial of therapy for patients with Fragile X syndrome. With a cut in the centers budget of 15% in FY 1987, it will not be possible to begin any of these collaborative studies. Limiting the centers program will also affect the training of young scientists who are being attracted to mental retardation research. This may slow the progress being made, especially in the area of molecular genetics, a very labor intensive field important to the prevention of over 200 hereditary causes of mental retardation. Reduced resources will also slow the developing collaborations between behavioral and biomedical scientists who are studying new areas of emphasis such as nongenetic intergenerational effects on retardation, and behavioral abnormalities that are caused by lower doses of chemical and environmental agents that, in high doses, are capable of producing structural malformations of the central nervous system.

In the Population Research Centers, too, the effect of reduced funding will be that very few new research initiatives will be undertaken. For example, we will not be able to establish the "external cores" planned as part of the contraceptive development initiative to foster interaction among the centers and take advantage of a particularly strong laboratory in one center to provide research support to other centers, rather than duplicating facilities. The long-run ramifications of this policy are that the speed of discoveries will be diminished, with consequent effect on the transfer of new basic science knowledge, such as the application of recombinant DNA methodology, to clinical practice.

In the program of Research for Mothers and Children, an effect will be upon the role of four centers proposed for a key role in the Institute's low birth weight initiative. The two centers that have just recently received grants for study of intrauterine growth retardation (IUGR)--the physiology of IUGR in animal models, and the mechanisms of fetal and neonatal growth--must start at a slower pace, in an area that requires stepped-up research efforts. Grants for two companion centers that would focus on prevention of premature labor and delivery cannot be awarded in either FY 1986 or FY 1987. The long-term effect will be to set a different tone for the low birth weight initiative which is designed as the most effective way to attack research needs on this most important problem in maternal and child health in the U.S. today.

Mr. Early. How will the reduction in the size and scope of the centers program affect NICHD's program plans--both immediate and long range?

Dr. Alexander. The immediate effect on the centers program is comparable to what we are experiencing in all other NICHD activities, as reductions for FY 1986 have been applied across the board to about the same degree. The result from lower funding levels in intramural research, extramural research project grants, and research training, as well as in the centers, is that somewhat less science will be accomplished, by fewer investigators who are supported by fewer team members and using less new equipment and more limited supplies. Thus, NICHD program plans would not change immediately, except to allow for not accomplishing as much as originally planned in starting new collaborations between centers for clinical trials, establishing sharing arrangements between centers for core resources, or adding new centers.

The long range effect would depend on the size and duration of program reductions. If the available resources do not go below anticipated levels for FY 1987, we should be able to maintain our emphasis on centers in essentially the same way that we do now. We would still depend upon them as multidisciplinary resources for attention to specialized research problems, and as an important complement to our highest extramural priority--the individual investigator initiated research project grant. In contrast, further reductions in funding would require reassessment of the centers concept in terms of how many to support, their resources in proportion to research project grants, and whether they would still be an effective mechanism to carry a lead role in major new activities such as the low birth weight initiative. The centers have been highly effective and efficient in all areas where we use them--Mental Retardation, Population, Low Birth Weight, and Perinatal Emphasis--and we would make every effort to sustain their successes.

Mr. Early. How many research centers will be up for renewal in FY 87?

Dr. Alexander. There are 14 research centers up for renewal in FY 1987.

Mr. Early. Provide the names and locations of all the Institute's research centers and indicate which ones will be up for renewal in FY 87.

Dr. Alexander. The following list provides the names and locations of the research centers currently funded by NICHD.

Population Research Centers

Grant Number	Title and Location
*P30 HD10003-11	Population Studies Center University of Michigan Ann Arbor, MI

**P30 HD05797-15	Center for Population and Reproductive Biology Research Vanderbilt University Nashville, TN
P30 HD05798-12	Carolina Population Center University of North Carolina Chapel Hill, NC
*P30 HD06160-16	Population Research Center University of Texas Austin, TX
**P30 HD06645-15	Center for Population Research Harvard University Boston, MA
P30 HD07495-14	Center for Population Research and Studies in Reproductive Biology Baylor College of Medicine Houston, TX
*P30 HD08610-12	Center for Research in Reproductive Physiology University of Pittsburgh Pittsburgh, PA
**P30 HD10202-10	Center for Research in Reproductive Biology University of Texas Health Science Center San Antonio, TX
**P30 HD10379-10	Population Studies Center University of Pennsylvania Philadelphia, PA
P30 HD18185-03	Reproductive Biology in Primates Oregon Primate Research Center Medical Research Foundation of Oregon Beaverton, OR
P30 HD18258-03	Center for the Study of Reproduction University of Michigan Ann Arbor, MI
P30 HD18288-04	Economic Analyses of the Family and Demographic Change National Opinion Research Center Chicago, IL
**P30 HD18968-03	The Laboratories for Reproductive Biology University of North Carolina Chapel Hill, NC
P30 HD05876-15	Center for Population Research University of Wisconsin Madison, WI

**P30 HD06268-12	Hopkins Population Center Johns Hopkins University Baltimore, MD
P30 HD08008-08	Population Research Center Princeton University Princeton, NJ
P30 HD11979-08	Reproductive Endocrinology Center Core Facilities University of California San Francisco, CA
P50 HD09140-12	Mode of Action of Reproduction Hormones Mayo Foundation, Rochester Rochester, MN
P50 HD09690-12	Neuroendocrinology of Reproduction and Growth Salk Institute for Biological Studies San Diego, CA
P50 HD12303-09	Pathophysiology of Premenstrual Syndrome University of California San Diego, CA
P50 HD12629-08	NICHD Population Research Center Studies in Reproductive Medicine University of Washington Seattle, WA
P50 HD12639-07	Center for Population Studies Rand Corporation Santa Monica, CA
**P50 HD13541-07	Specialized Population Research Center The Population Council New York, NY
P50 HD05077-16	Reproductive Biochemistry and Medicine Columbia University New York, NY

Mental Retardation Research Centers

Grant Number	Title and Location
**P30 HD02274-21	Research in Mental Retardation and Child Development University of Washington Seattle, WA
**P30 HD01799-22	Support for Mental Retardation Research Center Yeshiva University New York, NY

*P30 HD02528-20	Program for a Research Center in Mental Retardation University of Kansas Lawrence, KS
**P30 HD03110-20	Child Development and Mental Retardation University of North Carolina Chapel Hill, NC
P30 HD04024-18	Center Grant for Research in Mental Retardation University of Colorado Denver, CO
P30 HD04147-18	Research in Mental Retardation E. K. Shriver Center for Mental Retardation, Inc. Waltham, MA
P30 HD04612-18	Mental Retardation Research Center University of California Los Angeles, CA
**P30 HD18655-06	Mental Retardation Research Program Children's Hospital Corporation Boston, MA
**P30 HD03352-19	Wisconsin Center for Mental Retardation University of Wisconsin Madison, WI
**P30 HD04583-18	Core Grant for Mental Retardation University of Chicago Chicago, IL
P30 HD15052-07	Center for Research in Mental Retardation and Human Development Vanderbilt University Nashville, TN
**P01 HD17001-07	Biology of Down Syndrome University of California San Francisco, CA

Perinatal Emphasis Research Centers

Grant Number	Title and Location
P50 HD11089-08	Perinatal Studies of Disorders of Fetal Metabolism Case Western Reserve University Cleveland, OH
P50 HD11149-08	Initiation of Human Labor: Prevention of Prematurity University of Texas Health Science Center Dallas, TX

**P50 HD11343-09	Diabetes During Pregnancy: Effects on the Offspring Brown University Providence, RI
P50 HD13063-07	Fetal Hypoxia, Maternal Smoking and Newborn Outcome Columbia University New York, NY
P50 HD20748-02	Perinatal Emphasis Research Center University of Cincinnati Cincinnati, OH
P50 HD20761-02	Intrauterine Fetal Growth and Metabolism University of Colorado Denver, CO

Endocrinology, Nutrition and Growth Center

Grant Number	Title and Location
P30 HD22124-01	Nutrition and Chronic Disease Center University of California Berkeley, CA

* Up for renewal in FY 1986
** Up for renewal in FY 1987

CLINICAL TRIALS

Mr. Natcher. Provide a list of the clinical trials which will be under way in FY86 and indicate which ones are new.

Dr. Alexander. The following list indicates major ongoing clinical trials of the NICHD.

- Prevention of Cytomegalovirus (CMV) Disease
- Effects of Maternal PKU on Pregnancy Outcome
- Prematurity and Gestational Genitourinary Infections
- Intervention to Reduce Smoking During Pregnancy
- Effects of Tonsil-Adenoid Surgery on Throat Infection
- Extracorporeal Membrane Oxygenation (ECMO) in Newborn Respiratory Failure
- Strict Control of Diabetes in Pregnancy
- Clinical Studies on Human Milk
- Spermicides and Sexually Transmitted Diseases
- Phase II Clinical Studies with LHRH Agonists

- Human Biochemical Genetics
- Growth Hormone Releasing Factors
- Physiology of Puberty
- Mechanism of Pubertal Growth
- Protein Requirements of Infants and Children
- Iron Deficiency Anemia and Infant Behavior
- Perinatal Effects of Support During Labor
- Treatment Evaluation in Premenstrual Syndrome Patients
- Surfactant Biochemical Development and Stabilization
- Comparison of Chorion Villus Sampling and Amniocentesis
- Clinical Pharmacology of LHRH Antagonists
- L-Carnitine Treatment of Chronic Kidney Disease
- Development and Testing of Improved Spermicidal Contraceptives
- Prevention of Intrauterine Growth Retardation by Bed Rest
- Evaluation of a Polyvinyl Vaginal Contraceptive Sponge
- The Effect of Parent Weight on Obese Young Children
- Treatment of Obesity in Children and Adolescents
- Calcium and Phosphorus Nutrition in High Risk Infants
- Prevention of Otitis Media in Infants
- Treatment of Precocious Puberty and Other Endocrine Disorders with Leutinizing Hormone-Releasing Hormone
- Treatment of Infertility with Gonadotropin-Releasing Hormone in Men and Women.
- Effects of Growth Hormone Therapy on Children with Extreme Short Stature
- Intervention Strategies in Gestational Diabetes Mellitus

The following is a list of major new clinical trials in FY 1986.

- Parenteral Amino Acid Requirements in Low Birth Weight Infants
- Clinical Studies with Capronor Implantable Drug Delivery System
- Clinical Trial of New Drug Therapy in Treatment of Nephropathic Cystinosis

- Efficacy of Routine Ultrasound Screening in Pregnancy

- Effectiveness of Physical Therapy for Infants at Risk for Developmental Disabilities and Mental Retardation

- Pertussis Trials in Sweden

Mr. Early. Will you have to curtail any ongoing clinical trials with your FY86 revised budget request? If so, which ones?

Dr. Alexander. All of the ongoing clinical trials will be curtailed to the extent that the principal investigators find necessary under the negotiated reductions that we are making in grant awards this year--approximately 8% to 9% in project grants and 12% in center grants. In addition, the research networks of maternal-fetal medicine units and neonatal intensive care units will be able only to establish protocols for their clinical trials, but not to begin the trials in FY 1986 as originally planned. In each network, seven units will be funded instead of the intended ten.

Mr. Early. Doctor, will you have to curtail any ongoing clinical trials with your FY 87 budget request? If so, which ones?

Dr. Alexander. Ongoing clinical trials will continue, although at the negotiated reduced levels that we estimate for FY 1987--almost 10% for project grants and 14.5% for centers. Also, the two networks will continue with seven units each, instead of ten.

Mr. Early. Will you be able to start any new clinical trials in FY 87?

Dr. Alexander. The NICHD is planning to start some new clinical trials in FY 1987 at the President's budget level. These include:

- Studies on new long-acting injectable progestins to determine feasibility for use as a single injection, long-term contraceptive lasting 2-6 months.

- A trial to compare effects of different oral contraceptives on physiological indicators of cardiovascular disease risk using the recently marketed biphasic and triphasic oral contraceptives compared with more widely used low dose combined oral contraceptives.

- In the network of maternal-fetal medicine units, trials on management of the growth-retarded fetus, and management of pregnancies complicated by maternal diabetes and hypertension.

- In the network of neonatal intensive care units, trials on treatment for apnea (transient cessation of breathing) of prematurity, the efficacy of home monitoring of high risk infants and various therapies for significant asphyxia during the perinatal and neonatal periods.

Mr. Early. Are there any high priority clinical trials which are ready but cannot be initiated because of lack of funds in the FY 87 request? If so, please provide a list of these, along with a brief description and the associated costs, including first year costs.

Dr. Alexander. These high priority clinical trials would begin in FY 1987 if additional funds were available.

1. Effects of Growth Hormone Releasing Factors. This clinical trial will study the effects of repeated doses of chemically synthesized growth hormone releasing factors (GRF) on growth hormone deficient patients. GRF and its analogs hold great promise as an alternative to human growth hormone (GH), which is in limited supply, and may be contaminated with a potentially dangerous virus.
   First year cost: $500,000; Total cost: $2,000,000.

2. Nutrition, Other Factors, and the Outcome of Pregnancy. The project is identifying causal factors relating to pregnancy and poor pregnancy outcome among lower socioeconomic status inner city minority populations. The clinical trial that will result from this study will capitalize on this information and develop an intervention study to improve the pregnancy outcome in this group.
   First year cost: $150,000; Total cost: $600,000.

3. Clinical Trial on the Factors Influencing Breastfeeding. There is a need to analyze the causal factors of the low incidence of breastfeeding in certain populations in the U.S. and to develop intervention studies to improve both the incidence and duration of breastfeeding. This clinical trial is designed to address this critical problem.
   First year cost: $150,000; Total cost: $600,000.

4. Mental Retardation Research Centers (MRRCs) Network of Clinical Trials. The 12 MRRCs would form a network for collaborative clinical trials in the prevention or amelioration of mental retardation.
   First year cost: $1,200,000; Total cost: $6,000,000.

5. Clinical Trials of Pertussis Vaccine. A clinical trial will be undertaken in FY 1986 in Sweden, to test safety and efficacy. It would be necessary to expand this trial to the U.S. since the Swedish population is too small to detect rare side effects.
   First year cost: $2,200,000; Total cost: $8,400,000.

6. Clinical Trial of Hemophilus influenzae Vaccine. The bacteria Hemophilus influenzae is the most common cause of meningitis and a leading cause of acquired mental retardation in infants and young children despite antibiotics. A vaccine developed some years ago is effective only in older children (who are not the prime candidates for this disease). The newest vaccine appears to be effective in very young infants, but large clinical trials will be necessary to confirm efficacy and safety.
   First year cost: $500,000; Total cost: $1,500,000.

7. Clinical Studies with a Long-Acting Spermicidal Formulation. A long-acting (24 hr.) spermicidal formulation releasing nonoxynol

has been prepared. Assuming that the initial studies are encouraging a clinical trial would be initiated in FY 1987.
First year cost: $150,000; Total cost: $350,000.

8. Clinical Trials Within the Network of Maternal/Fetal Medicine Units. Additional trials would test the use of medications to treat various maternal diseases, and the safety and efficacy of various therapeutic agents to stop premature labor.
First year cost: $500,000; Total cost: $2,500,000.

9. Clinical Trials within the Network of the Neonatal Intensive Care Units. Additional trials would examine some of the current treatments in the long-term management of bronchopulmonary dysplasia, and the use of anticonvulsants in the treatment of neonatal seizures.
First year cost: $500,000; Total cost: $2,500,000.

SMALL BUSINESS INNOVATIVE RESEARCH

Mr. Early. Doctor, briefly would you tell us how your Institute is using the Small Business Innovative Research Program?

Dr. Alexander. The Institute has addressed the Small Business Innovative Research (SBIR) program by outlining in both grant and contract solicitations certain priority areas that can be successfully pursued by small business organizations. In our contraceptive development program, several projects have been funded for the preliminary phase and a smaller number for the more extensive product development phase. Examples include efforts toward synthesis of new contraceptive drugs, new spermicides, transdermal delivery of contraceptive drugs and development of methods for the detection of drugs and hormones in body fluids.

The SBIR program is also being used successfully in pediatric research. The most notable example is the development of a non-invasive mechanical device that generates vibrations and sound for use in a baby's crib. Data generated in clinical studies show that the conditions developed will significantly reduce colic in infants. Infant colic remains a syndrome of unknown etiology, even though there have been many investigations into its cause and cure. In addition to the obvious discomfort to the infant, it causes considerable stress and anxiety in the family of the affected infant. Thus, colic itself and the family side effects contribute significantly to medical costs during infancy. Additionally, the stressful aspects of colic have been associated, in some cases, with child abuse and neglect. Because this device reduces markedly the crying and agitated state of the colicky infant, it will probably reduce the frequency of doctor visits associated with the syndrome and may also have the effect of reducing the potential for abuse of the colicky infant.

Other examples include development of computerized systems for diagnosis and remediation of dyslexia, and development of a new type of infant apnea monitor.

RESEARCH AND DEVELOPMENT CONTRACT MECHANISM

Mr. Early. Would you give us a few examples of how the Institute utilizes its research and development contract mechanism?

Dr. Alexander. The NICHD is very selective in its use of the contract mechanism. It is used to stimulate new areas of research and to provide a needed service or resource to the scientific community that cannot be accomplished by any other support mechanism. An example of the former use is a series of contracts that have been recently awarded to develop new methods for the analysis of human milk. Human milk is important as a nutrient source in the clinical management of very low birth weight infants. It also has properties that protect these infants from infection as well as other biological properties that are important for normal development. Unfortunately, many of the methods used to analyze human milk before it can be used in the clinic are either archaic or inaccurate. The need was seen for modern methods that are quick, accurate and inexpensive; thus this contract effort was undertaken.

A prime example of providing a resource for other scientific projects is a contract establishing a human DNA probe repository. Recombinant DNA technology has provided the scientist with an enormously powerful tool for investigating the functions of the living cell. In order to share these technical advances among scientists, a repository of defined genetic material (DNA probes) was established. This endeavor will greatly increase the availability of DNA probes and will markedly benefit the research programs of NIH.

The contract mechanism is particularly important in our population research program, where contracts are best suited for projects that are identified by the NICHD, rather than initiated by investigators in the field, in the areas of contraceptive development and contraceptive evaluation. Examples in contraceptive development include the development of new drugs, such as steroid combinations for male contraception; improved methods of drug delivery, such as long-acting implants and injectables; and improved barrier methods, such as the cervical cap and variations of the diaphragm. Examples in contraceptive evaluation are surveillance studies, clinical trials, and epidemiological studies on such topics as whether there is an association between reproductive system cancer and long-term exposure to oral contraceptives; intrauterine devices (IUDs) and their role in the occurrence of undesired infertility; and long-term health effects of both male and female sterilization.

ADDITIONAL FUNDING

Mr. Early. If an increase over the FY 87 request is provided, how would you use these additional funds?

Dr. Alexander. Our priority for additional funds over the FY 1987 request would be used to invest more in our two major initiatives for research on low birth weight and contraceptive development, and to increase support in other areas where we have immediate opportunity to capitalize on new findings in basic science or to move closer to clinical application of what we have already learned.

In the low birth weight initiative, the most pressing need is to expand the level of effort in the networks of maternal-fetal medicine units and neonatal intensive care research units. We would add three units in each network and increase the number of clinical trials that could be started in each. We would also add two new centers focused on prevention of premature labor and delivery. These activities would be complemented by epidemiological studies on ethnic differences in the rate of low birth weight, and a number of individual special projects on such topics as identifying causal factors relating to pregnancy and poor pregnancy outcome among lower socioeconomic status inner city minority populations.

In the contraceptive development initiative, we would emphasize studies on the recently characterized protein inhibin that may lead to improved contraception for both men and women, further research on various brain hormones and immunologic aspects of reproduction that have implications for both contraception and infertility, and a clinical trial on a new long-acting spermicidal formulation. Other high priorities that would require additional funds include clinical trials of long-acting injectable contraceptives, and studies of teenage pregnancy, particularly regarding behavioral aspects of the decision making process on use or non-use of contraception. Also in the area of clinical trials, our Mental Retardation Research Centers would receive additional funds for collaborative efforts on prevention or amelioration of mental retardation.

NICHD intramural scientists require additional funds to carry out U.S. field trials of the pertussis vaccine they have developed, as a follow up to preliminary trials to be conducted this summer in Sweden, and their new H. influenzae vaccine that has the potential to eliminate the major cause of acquired mental retardation in this country. Other intramural needs are for replacing outdated equipment and restoring supplies of research materials and supporting services to previous levels.

To strengthen the foundation for attracting enough of the best young people in biomedical research, we would increase the number of Physician Scientist and Clinical Investigator Awards and restore research training to FY 1985 levels. In terms of mechanisms of research support in both population research and research for mothers and children, we would fund about 174 additional competing research project grants and restore full funding to project grants and centers.

RESEARCH INITIATIVES

Mr. Early. Will any significant new research initiatives or opportunities be lost or delayed by lack of funds in the FY 87 budget?

Dr. Alexander. Yes. Although the NICHD will be able to support some new research initiatives in FY 1987, others will be delayed at the requested funding level.

Mr. Early. Please provide for the record a list of these, along with a brief description and the funding requirements associated with each.

Dr. Alexander. The following new projects will be postponed:

Low Birth Weight (LBW) Initiative

° Establishment of two new centers focused on the mechanisms responsible for intrauterine growth retardation (IUGR) (particularly pregnancy-induced hypertension or pre-eclampsia) and their treatment, and the mechanisms for premature labor and its prevention.

° Epidemiologic studies addressing IUGR and preterm delivery across generations, the components of prenatal care that are most effective in prevention of LBW, and the relation of maternal seroconversion for certain bacteria during pregnancy to LBW.

° Intramural research on fetal growth factors in relation to IUGR, and the role of angiotensin receptor abnormalities in pregnancy-induced hypertension and LBW.

° Clinical Trials within the Network of Maternal/Fetal Medicine Units. Additional trials would test the use of medications to treat various maternal diseases, and the safety and efficacy of various therapeutic agents to stop premature labor.

° Clinical Trials within the Network of Neonatal Intensive Care Units. Additional trials would examine some of the current treatments in the long-term management of bronchopulmonary dysplasia, and the use of anticonvulsants in the treatment of neonatal seizures.

Additional funds required in FY 1987: $11.1 million

Contraceptive Development Initiative

° Studies on inhibin, a protein that offers great promise in the development of new, natural contraceptives, as well as a possible key to understanding infertility.

° Studies of immunocontraception, new reproductive peptide hormones, and vulnerable steps in the reproductive process.

° Behavioral studies on early childbearing, critical because a major proportion of the nation's unintended pregnancies occur among teenagers.

° Clinical studies with a long-acting (24 hour) spermicidal formulation.

° Studies of the safety and efficacy of certain contraceptive methods.

- Research on the acceptability and utilization of contraceptive methods.

Additional funds required in FY 1987: $11.7 million

Mental Retardation

- Delayed funding of clinical trials in mental retardation research centers, on prevention and amelioration of mental retardation, including the testing of dietary treatment of mental retardation.

- Plans for "external core facilities" by which one center would specialize in a new procedure or study method and make this resource available more efficiently, and at lower cost, to other centers.

Additional funds required in FY 1987: $2.7 million

Mr. Early. Doctor, will any significant research initiative currently under way be halted or seriously delayed due to FY 87 funding levels?

Dr. Alexander. No initiatives begun in FY 1986 will have to be halted in FY 1987. Some initiatives, however, will have to continue at lower levels of funding than were originally planned.

Mr. Early. To what extent will there be major reductions in the scope of ongoing or new initiatives because of the FY 87 funding levels? For the record, please provide a list of these along with a brief description and the amounts associated with each initiative.

Dr. Alexander. The following projects will continue at lower levels of funding:

Low Birth Weight Initiative

- As part of its special initiative on low birth weight research, the Institute had planned to establish a national network of ten rather than seven maternal-fetal medicine units, and a companion network of ten rather than seven neonatal intensive care units. A 30% reduction in the number of maternal-fetal medicine units will mean 10,000-15,000 fewer high-risk pregnancies to be studied and consequent delay in implementation of new methods to prevent low birth weight. A 30% reduction in the number of neonatal intensive care units means approximately 1,500 fewer premature infants to be studied, with resulting delay in application of new treatment methods.

- A clinical trial to assess the value of routine obstetric ultrasound screening in detecting and managing intrauterine growth retardation is scheduled to begin in FY 1986. This trial will continue in FY 1987, but will be reduced in scope.

Pertussis

- NICHD scientists have recently developed a new pertussis vaccine which they believe will be much safer and more effective than the DPT innoculations currently administered. A field trial originally scheduled to be conducted in the State of Massachusetts during FY 1987 will have to be postponed.

Additional funds required in FY 1987: $2.8 million

COMPUTER PROGRAM FOR DIABETIC ADOLESCENTS

Mr. Early. Would you briefly explain the computer program which has been developed for use by diabetic adolescents to better control the management of their disease.

Dr. Alexander. The level of blood sugar that the body needs and tolerates is carefully regulated by a number of hormones, the most important of which is insulin. These hormones work together to respond to outside events which can change the level of blood sugar, such as exercise, stress, fever, and changes in dietary intake. To replace the missing insulin in diabetics with a precision that approximates the body's own "wisdom," it is necessary to consider these outside events, as well as the level of blood sugar, on a day-to-day and sometimes hour-to-hour basis. This kind of tight management, which may prolong life and improve health, is aided greatly by our new computer program which can easily be used by teenagers with access to a home or school computer. The new computer program permits the rapid integration of all the variable events that can influence the health of the diabetic patient. Since one of the main problems in managing chronic illness in adolescents is that they often rebel against control, even when it is in their own best interest, putting the management of diabetes more directly into the hands of the adolescent himself should promote compliance and reduce the family stress that often occurs with this disease.

CONTRACEPTIVE DEVELOPMENT INITIATIVE

Mr. Porter. The Center for Population Research is one of the world's most important sources of contraceptive research, information and technology in the field. I understand that there are plans for expanded research in contraceptive development -- namely, the contraceptive development initiative. Could you elaborate on the plans for the contraceptive development initiative?

Dr. Alexander. The major features of the contraceptive development initiative involve research in four areas: (1) basic research on human reproduction which can identify new fertility regulation approaches; (2) applied research in contraceptive development; (3) assessment of safety and efficacy of existing methods of contraception; and (4) research on the behavioral aspects of contraceptive use.

The goals of the basic research component are to provide leads for the development of a new generation of modalities for fertility regulation through research on the following topics: immunology related to contraception; the prevention of gamete maturation; the discovery of new substances in the body that may have contraceptive potential; blockade of the action of the primary fertility hormones in the body; identification of steps in reproductive processes that are vulnerable to interdiction; and the application and introduction of new and highly sophisticated technologies into research related to contraception.

In the applied area of contraceptive development, the Institute is currently supporting several clinical trials involving new drugs and devices that may prove to be attractive to various segments of the population. At the laboratory level we are pursuing synthesis and testing of new drugs, development of new barrier methods, development of new methods of drug administration, and the development of antifertility vaccines.

Research on the safety and efficacy of existing contraceptive methods would include studies of methods used in foreign countries but not approved for use in the United States, modifications of IUD's that may make them safer, and studies of the effects of recent formulations of oral contraceptives on various aspects of women's health, including the risk of cardiovascular disease, cancer, and indicators of overall mental and physical health.

Research in the demographic and behavioral sciences would include studies of factors tending to encourage or discourage the use of various methods of fertility control. These would include studies of the acceptability and probable utilization of proposed new methods; the choice, effectiveness, and continuation of use of existing methods; and the strength of motivation for preventing pregnancy.

Mr. Porter. Do you have sufficient funds to proceed with all parts of the contraceptive development initiative?

Dr. Alexander. We will be able to proceed with some important components of the contraceptive development initiative, including those involving basic research, contraceptive development, and studies of factors affecting the use of contraceptive methods.

Mr. Porter. What effects will the Gramm-Rudman cuts have?

Dr. Alexander. The Gramm-Rudman-Hollings legislation reduced the NICHD appropriation by 4.3% across-the-board, affecting the principal funding mechanisms of research grants, research contracts, and centers. All of these mechanisms are used in undertaking the contraceptive development initiative, and the impact of budget changes will be approximately the same for all components of the initiative.

Mr. Porter. Will there be parts of the initiative that you cannot fund in 1986 and 1987?

Dr. Alexander. Yes. Although the initiative has begun, there will be some projects that are delayed or reduced in scope in 1986 and 1987. Examples are:

- Studies of immunocontraception
- Clinical trials of new long-acting injectables
- Inability to follow up on the recent isolation of inhibin, a protein that offers great promise in the development of new, natural contraceptives, as well as a possible key to understanding some types of infertility
- Studies of teenage pregnancy, particularly regarding behavioral aspects of the decision-making process on use or non-use of contraception

Mr. Porter. In your professional judgment, what funds will be required to support all parts of this important effort?

Dr. Alexander. In my professional judgment, support for all parts of the contraceptive development initiative would require additional amounts of $9.9 million in FY 1986 and $11.7 million in FY 1987.

Mr. Porter. Is there any relationship between the contraceptive development initiative and the prevention of low birth weight and infant mortality?

Dr. Alexander. The contraceptive development initiative is seeking to improve people's ability to control their fertility, that is, prevent unintended pregnancies. We know that unwanted/mistimed pregnancies are more likely to be associated with consequent poor prenatal care and adverse outcomes such as low birth weight, as well as a higher incidence of infant mortality. We view these two initiatives as interactive and complementary--reducing the incidence of unintended pregnancy is a major component of an effort to reduce low birth weight and infant mortality.

Mr. Porter. What evidence is there that the use of improved contraceptives would save babies' lives?

Dr. Alexander. Research shows that women who have births resulting from pregnancies that were mistimed or unwanted are less likely to receive adequate prenatal care. Inadequate prenatal care is associated with an increased risk of bearing a low birth weight baby. Low birth weight, in turn, is an important risk factor for infant mortality. In addition, we know that women who are at risk of an unwanted pregnancy are also considered high risk for poor pregnancy outcome and reduced infant survival. There may be many factors linking the two, including poverty, poor maternal education and inadequate health services.

Mr. Porter. What, if anything, does the contraceptive development initiative attempt to do in the area of teen pregnancy?

Dr. Alexander. The Institute has a very active program of research on teen pregnancy, and this subject has highest priority in the behavioral component of the Initiative. Teens in the U.S. are using contraception, but not always early enough after they initiate sexual activity, not always regularly enough and not always with the most effective methods. We have issued a request for grant applications (RFA) as part of the contraceptive development initiative for studies that will build on earlier exploratory work and provide more complete information about the use of contraception among teenagers. Several projects from this RFA will be funded in FY 1986.

Mr. Porter. Are there any cost-savings associated with the contraceptive development initiative? On a per capita basis? On an aggregate basis?

Dr. Alexander. Development of improved methods of fertility regulation is a high-risk and expensive process. However, the costs associated with unplanned or unwanted pregnancies are many-fold higher when we consider that over three million pregnancies fall into these categories. An unplanned or unwanted pregnancy has adverse health effects on both the mother and the child and frequently imposes an economic burden on the family. It is well documented that the availability of numerous types of contraceptive products increases overall contraceptive utilization. Consequently, new products that are developed under the Initiative should provide both the individual and society with reduced incidence of unplanned and unwanted pregnancies and result in substantial cost savings. The Alan Guttmacher Institute conducted a study that used simulation methods to estimate the effects on public assistance costs of preventing unplanned births and of various policy interventions. This study estimated a reduction in public assistance of [illegible] million in one year as a result of improved fertility regulation.

Mr. Porter. What studies do you plan to undertake in order to investigate the spectrum of short- and long-term cost-savings associated with the contraceptive research initiative?

Dr. Alexander. We funded the study cited above and will continue to support high quality research which addresses such important policy questions. The results of such studies certainly demonstrate the economic value of improved contraception, but there are many other benefits, such as improvements in mental and physical health and reductions in induced abortions.

[illegible]

[illegible]

[illegible]

[illegible]

[illegible]

[illegible]

[illegible]

overemphasize the seriousness of this problem. If the Institute and its contractors are not able to solve the issue of product liability insurance coverage, we will be unable to do the clinical testing required to bring products to the market and our contraceptive development program will come to a halt.

CONTRACEPTIVE SAFETY

Mr. Porter. A 1985 Gallup poll indicated that 76% of women in the United States believe that use of the birth control pill is dangerous. Are these fears justified?

Dr. Alexander. No. Misinformation about the safety of oral contraceptives (OCs) is widespread and profound. For example, of women in the Gallup poll who considered OCs dangerous, about one-third believed they are a cause of cancer. The major issues here refer to cancer of the breast and reproductive tract (uterus and ovary). A wide range of studies has consistently shown that the types of OCs currently in use actually decrease women's risk of cancer of the endometrium (uterine lining) and ovary. The world's largest and most thorough study of OCs and breast cancer is the Cancer and Steroid Hormone Study, which was initiated by the NICHD and conducted through an interagency agreement with the Centers for Disease Control. This study shows no significant effect of OC use on the risk of breast cancer, even for women with long-term use that began before 25 years of age. Use of OCs may increase susceptibility to dysplasia of the uterine cervix (vaginal opening of the uterus), and, if left untreated, dysplasia has potential for eventually progressing to cancer. However, annual examination of the cervix with Pap smears is very reliable for early diagnosis of dysplasia, and curative methods of treatment are widely available which require only limited surgery.

Mr. Porter. Is your Institute conducting any studies as to the safety of the pill?

Dr. Alexander. Yes. The NICHD Contraceptive Evaluation Branch is currently conducting 14 studies to further investigate and improve the safety of the pill, and four new projects are scheduled for initiation in FY 1987 if sufficient funds are available. For example, the main danger to health for women using OCs in the 1960's-1970's was an increased risk of cardiovascular disease (heart attacks, strokes, and blood clots in veins). This appears to have been due largely to use of unnecessarily large doses of estrogen and progestogen (the female sex hormones in OCs), and dosage has since been greatly reduced. Therefore, a major component of the current and anticipated new research referred to above is focused on re-evaluating the risk of cardiovascular disease for women using the newer low-dose OCs.

Mr. Porter. Is the NICHD currently conducting any studies on the safety of the IUD?

Dr. Alexander. Not currently. Studies previously conducted by the NICHD Contraceptive Evaluation Branch, and published in April 1985, show that use of intrauterine devices (IUDs) by women who have had no children, and who have more than one sexual partner, substantially increases their risk of infertility from damage to the fallopian tubes (the channels through which eggs pass from the ovary to the uterus). This occurs because sexually transmitted diseases (such as gonorrhea) can seriously damage the fallopian tubes, and the presence of an IUD in the uterus evidently increases susceptibility to such diseases. Since April 1985, the IUDs most widely used in this country (the Lippes loop and Copper 7) have been withdrawn from the market.

PROFESSIONAL JUDGMENT OF RESOURCES

Mr. Porter. In your professional judgment, what else needs to be done that the NICHD is uniquely qualified to do?

Dr. Alexander. In addition to the contraceptive development initiative, we would give highest priority to expanding the level of effort under our low birth weight initiative. Here the most pressing need is to add three units each in the research networks of maternal-fetal medicine units and neonatal intensive care units, and to increase the number of clinical trials that can be started in both networks in FY 1987. Additional trials would test the use of medications to treat various maternal diseases; the safety and efficacy of different therapeutic agents to stop premature labor; current treatments in the long-term management of bronchopulmonary dysplasia; and the use of anticonvulsants in the treatment of neonatal seizures. As a companion effort to the recent establishment of two centers focusing on the problem of intrauterine growth retardation, two other center grants would be awarded to address the prevention of premature labor and delivery. These activities in the low birth weight initiative would be complemented by epidemiological studies on ethnic differences in the rate of low birth weight, and a number of individual special projects on such topics as identifying causal factors relating to pregnancy and poor pregnancy outcome among lower socioeconomic status inner city minority populations.

The mental retardation research centers, which comprise the most important component of our program in mental retardation and developmental disabilities, are prepared to undertake new collaborative efforts for clinical trials on prevention or amelioration of mental retardation.

The NICHD is in a unique position on the development of new vaccines that have potential to eliminate pertussis (whooping cough), *H. influenzae* infection that causes meningitis (the major cause of acquired mental retardation in the U.S.) and typhoid fever. Institute intramural scientists have developed vaccines for each of these diseases, and preliminary clinical trials are being carried out. Critical next-steps of larger U.S. trials of the pertussis and *H. influenzae* vaccines will be delayed, however, for lack of resources in the coming year.

From the base of new initiatives and previous scientific accomplishment supported by the NICHD in population research and research on the special health problems of mothers, children, and families, the Institute also has an important opportunity to strengthen the foundation for attracting enough of the best young people in science into research careers in these fields.

Particularly, we would look toward more emphasis on the Physician Scientist and Clinical Investigator Awards, and the restoration of research training support to FY 1985 levels.

Mr. Porter. In your professional judgment, what additional funds would be required to support these efforts?

Dr. Alexander. For FY 1987, in addition to the $11.7 million already identified for the contraceptive development initiative, our requirements would be $11.1 million for the low birth weight initiative; $2.7 million for the mental retardation research centers; and $2.8 million for the pertussis and H. influenzae vaccine trials. Providing comparable levels of support for other parts of the NICHD total program, including the higher level of research training, an additional 174 competing research project grants, restoration of full funding to both research project grants and research centers, and restoration of intramural research support to previous levels, would bring the increase for FY 1987 to approximately $67 million over the request.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

National Institute of Child Health and Human Development

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NATIONAL INSTITUTES OF HEALTH

National Institute of Child Health and Human Development

For carrying out section 301 and Title IV of the Public Health Service Act with respect to child health and human development, [$321,972,000] *$309,119,000. (Department of Health and Human Services Appropriation Act, 1986.)*

NATIONAL INSTITUTES OF HEALTH

National Institute of Child Health and Human Development

Amounts Available for Obligation [1]

	1985	1986	1987
Appropriation.................	$313,295,000	$321,972,000	$309,119,000
Enacted administrative reduction..................	—	-176,000	—
Sequester order...............	—	-13,838,000	—
Proposed rescission...........	—	-1,150,000	—
Subtotal, adjusted appropriation.............	313,295,000	306,808,000	309,119,000
Comparative transfer to:			
National Cancer Institute for changes in the Central Services financing mechanisms and formulas.....	-2,755,000	—	—
Subtotal, adjusted budget authority........	310,540,000	306,808,000	309,119,000
Unobligated balance, start of year................	—	+486,000	—
Unobligated balance, end of year..................	-486,000	—	—
Unobligated balance, lapsing..	-231,000	-215,000	—
Total obligations...........	312,578,000	307,079,000	309,119,000

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[1] Excludes the following amounts for reimbursable activities carried out by this account: 1985 -- $701,000; 1986 — $676,000; 1987-- $1,146,000, of which $700,000 is for AIDS research.

National Institute of Child Health and Human Development

Budget Mechanism
(Dollars in thousands)

Research Grants	1986 1/ Appropriation No.	1986 1/ Appropriation Amount	1986 Available after sequestering 1/ 2/ No.	1986 Available after sequestering 1/ 2/ Amount	1986 Revised 1/ 2/ No.	1986 Revised 1/ 2/ Amount	1987 No.	1987 Amount
Research Projects:								
Noncompeting projects.......	891	$130,271	891	124,669	891	123,919	913	125,465
Admin. supplementals........	(40)	1,272	(40)	1,217	(40)	1,217	(40)	1,340
Competing:								
Renewal....................	182	33,038	182	31,631	176	31,434	155	28,031
New........................	293	34,101	293	32,621	283	32,432	294	34,270
Supplemental...............	8	529	8	527	8	513	7	525
Subtotal, competing.....	483	67,668	483	64,779	467	64,379	456	62,826
Subtotal, research projects...	1,374	199,211	1,374	190,665	1,358	189,515	1,369	189,631
Research Centers:								
Specialized/comp. centers...	43	27,538	43	26,355	43	26,355	43	26,217
Subtotal, research ctrs...	43	27,538	43	26,355	43	26,355	43	26,217
Other Research:								
Research career program.....	110	6,059	105	5,798	105	5,798	105	5,798
Minor. biomed. res. support.		589		564		564		564
Other research related......	8	962	8	921	8	921	8	921
Subtotal, other research..	118	7,610	113	7,283	113	7,283	113	7,283
Total, Research Grants....	1,535	234,359	1,530	224,303	1,514	223,153	1,525	223,131

Training								
Individual awards								
Noncompeting..............	80	1,967	80	1,967	80	1,967	62	1,633
Competing								
Renewal................	--	--	--	--	--	--	--	--
New....................	23	583	19	473	19	473	33	718
Subtotal, individ.....	103	2,550	99	2,440	99	2,440	95	2,351
Institutional awards								
Noncompeting..............	504	9,958	504	9,958	504	9,958	473	9,477
Competing								
Renewal................	46	955	42	905	42	905	66	1,272
New....................	21	438	--	--	--	--	--	--
Subtotal, inst........	571	11,351	546	10,863	546	10,863	539	10,749
Total, training..........	674	13,901	645	13,303	645	13,303	634	13,100
Research and Development Contracts....................	109	23,152	106	22,156	106	22,156	106	22,156
Intramural Research............		35,733		33,981	FTE 255	33,981	FTE 255	35,746
Research Management and Support.................		15,137		14,486	164	14,486	164	14,986
Total, NICHD..................		322,282		308,229		307,079		309,119

Note: 1/ Reflects an enacted administrative reduction of $176,000 and a carryover in unobligated funds of $486,000.

2/ Reflects a consultant services (Section 515 of the Treasury-Postal Service Appropriation Act, 1985) withholding of $215,000.

NATIONAL INSTITUTES OF HEALTH

National Institute of Child Health and Human Development

CROSSWALK - 1986 Appropriation[1/]

(Dollars in thousands)

	MECHANISM								
	Research Grants			Training Programs					
PROGRAM ACTIVITY	Research Projects	Research Centers	Other Research	Individual	Institutional	Research and Development Contracts	Intramural Research	Research Management and Support	Total
Research for mothers and children..........	$128,898	$13,973	$5,395	$1,631	$8,155	$7,437			$165,489
Population..............	70,313	13,565	2,215	919	3,196	15,715			105,923
Intramural research....							35,733		35,733
Research management and support...........								15,137	15,137
Total...........	199,211	27,538	7,610	2,550	11,351	23,152	35,733	15,137	322,282

[1/] Reflects an enacted administrative reduction of $176,000 and a carryover in unobligated funds of $486,000.

NATIONAL INSTITUTES OF HEALTH

National Institute of Child Health and Human Development

CROSSWALK - 1987 Congressional Justification

(Dollars in thousands)

	MECHANISM								
	Research Grants			Training Programs		Research and Development Contracts	Intramural Research	Research Management and Support	Total
PROGRAM ACTIVITY	Research Projects	Research Centers	Other Research	Individual	Institutional				
Research for mothers & children.	$122,268	$13,303	$5,045	$1,501	$7,722	$7,120			$156,959
Population............	67,363	12,914	2,238	850	3,027	15,036			101,428
Intramural research..							35,746		35,746
Research management and support.........								14,986	14,986
Total............	189,631	26,217	7,283	2,351	10,749	22,156	35,746	14,986	309,119

NATIONAL INSTITUTES OF HEALTH

National Institute of Child Health and Human Development

CROSSWALK - 1986 Revised Estimate[1/] [2/]

(Dollars in thousands)

	MECHANISM								
	Research Grants			Training Programs					
PROGRAM ACTIVITY	Research Projects	Research Centers	Other Research	Individual	Institutional	Research and Development Contracts	Intramural Research	Research Management and Support	Total
Research for mothers & children.	$122,370	$13,373	$5,045	$1,560	$7,804	$7,120			$157,272
Population............	67,145	12,982	2,238	880	3,059	15,036			101,340
Intramural research..							33,981		33,981
Research management and support.........								14,486	14,486
Total............	189,515	26,355	7,283	2,440	10,863	22,156	33,981	14,486	307,079

[1/] Reflects an enacted administrative reduction of $176,000 and a carryover in unobligated funds of $486,000.

[2/] Reflects a consultant services (Section 515 of the Treasury-Postal Service Appropriation Act, 1985) withholding of $215,000.

NATIONAL INSTITUTES OF HEALTH

National Institute of Child Health and Human Development

CROSSWALK - 1986 Available After Sequestering [1] [2]

(Dollars in thousands)

PROGRAM ACTIVITY	MECHANISM: Research Grants: Research Projects	Research Grants: Research Centers	Research Grants: Other Research	Training Programs: Individual	Training Programs: Institutional	Research and Development Contracts	Intramural Research	Research Management and Support	Total
Research for mothers & children	$123,370	$13,373	$5,063	$1,560	$7,006	$7,120			$157,972
Population	67,305	12,952	2,230	880	5,059	17,936			101,750
Intramural research							33,901		33,901
Research management and support								14,606	14,606
Total	190,665	26,325	7,283	2,440	13,065	25,136	33,901	14,606	308,229

[1] Reflects an enacted administrative reduction of $170,000 and a carryover in unobligated funds of $686,000.

[2] Reflects a consultant services (Section 515 of the Treasury-Postal Service Appropriation Act, 1985) withholding of $213,000.

National Institute of Child Health and Human Development

Summary of Changes

1986 Current estimated obligations	[illegible]
1987 Estimated obligations	[illegible]
Net Change	[illegible]

	1986 Base	Change from Base
Increases:		
A. Built-in:		
1. Within-grade increases	[illegible]	[illegible]
2. Federal Employees Compensation Fund increase	[illegible]	[illegible]
3. FTS rate increase	[illegible]	[illegible]
4. Payment for centrally furnished services	[illegible]	[illegible]
5. Increased cost of laboratory supplies, materials and other expenses	[illegible]	[illegible]
Subtotal		[illegible]
B. Program:		
1. Research project grants:		
a. Noncompeting continuations converting from competing status	[illegible]	[illegible]
b. Competing (new, renewals and supplementals)	[illegible]	[illegible]
c. Increase in administrative supplements	[illegible]	[illegible]
2. Research centers:		
a. Noncompeting continuations converting from competing status	[illegible]	[illegible]
b. Competing (new and renewals)	[illegible]	[illegible]
3. Other research:		
a. Noncompeting continuations converting from competing status	[illegible]	[illegible]
b. Competing (new and renewals)	[illegible]	[illegible]

[illegible]

	[illegible]	[illegible]
[illegible]		
[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]
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[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]

Summary of Changes -- continued

	1986 Base	Change from Base
4. Individual training awards:		
a. Noncompeting completed or converting to competing status........................	$1,967,000	-$807,000
b. Competing completed or converting to non-competing status.............	473,000	-473,000
5. Institutional training awards:		
a. Noncompeting completed or converting to competing status........................	9,958,000	-1,386,000
b. Competing completed or converting to non-competing status.............	905,000	-905,000
Total, decreases......................		-136,262,000
Total, net change........................		+2,040,000

National Institute of Child Health and Human Development

Budget Authority by Activity
(Dollars in thousands)

	1986 Appropriation	1986 Available after sequestering	1986 Revised		1987	
	Amount	Amount	FTEs	Amount	FTEs	Amount
Research for mothers and children.......	$165,489	$157,972	--	$157,272	--	$156,959
Population.......	105,923	101,790	—	101,340	—	101,428
Intramural research.......	35,733	33,981	255	33,981	255	35,746
Research management and support....	15,137	14,486	164	14,486	164	14,986
Total obligations....	322,282	308,229	419	307,079	419	309,119
Unobligated balance, start of year........	-486	-486		-486		---
Unobligated balance lapsing........	---	215	—	215	---	---
Total............	321,796	307,958	419	306,808	419	309,119

Note: All 1986 columns reflect an enacted administrative reduction of $176,000.

National Institute of Child Health and Human Development

Obligations by Object

	1985 Actual	1986 Estimate	1987 Estimate
Total number of full-time permanent pos.	386	386	386
Total compensable workyears:			
Full-time equivalent employment.......	454	441	441
Full-time equivalent of overtime and holiday hours..................	5	5	5
Average ES salary......................	$66,232	$66,232	$62,232
Average GS grade.......................	9.14	9.14	9.14
Average GS salary......................	$28,224	$28,224	$28,224
Average salary, grades established by act of July 1, 1944 (42 U.S.C. 207)......................	35,361	35,361	35,361
Average salary of ungraded positions...	23,206	23,206	23,206
Personnel compensation:			
Permanent positions..................	$11,043,000	$11,485,000	$11,675,000
Positions other than permanent.......	3,692,000	3,729,000	3,765,000
Other personnel compensation.........	584,000	602,000	632,000
Special personnel services...........	1,203,000	1,320,000	1,320,000
Subtotal, personnel compensation.	16,522,000	17,136,000	17,392,000
Personnel benefits.....................	2,151,000	2,305,000	2,340,000
Benefits for former personnel..........	28,000	36,000	36,000
Travel and transportation of persons...	726,000	825,000	825,000
Transportation of things...............	92,000	95,000	95,000
Rent, communications and utilities.....	1,103,000	1,150,000	1,150,000

Obligations by Object — continued

Printing and reproduction	499,000	525,000	525,000
Other services:			
Project contracts	23,040,000	22,156,000	22,156,000
Centrally furnished services	15,876,000	12,849,000	13,028,000
Standard level user charge	416,000	549,000	602,000
Other	8,266,000	5,997,000	7,739,000
Supplies and materials	5,039,000	5,000,000	5,000,000
Equipment	2,248,000	2,000,000	2,000,000
Lands and structures	23,000	—	—
Grants, subsidies & contributions	236,547,000	236,456,000	236,231,000
Interest and dividends	2,000	—	—
Total	312,578,000	307,079,000	309,119,000

National Institute of Child Health and Human Development

Significant Items in Senate Appropriations Committee Report

Item	Action Taken or to be Taken
1986 Senate Report	
Low Birth Weight	
1. The Committee has restored funding for low birth weight research and directs the Institute to continue to give this research program its highest priority.	1. In FY 1985 the NICHD began implementing an enhanced research program focused on the prevention of low birth weight and infant mortality. In FY 1986 this initiative continues to be among the Institute's highest priorities. Funding for low birth weight research in FY 1986 will include support for a network of maternal/fetal medicine units, and another network of neonatal intensive care units.

NATIONAL INSTITUTES OF HEALTH
National Institute of Child Health and Human Development

Authorizing Legislation

	PHS Act/ Other Citation	U.S. Code Citation	1986 Amt. Authorized	1986 Revised Estimate	1987 Amt. Authorized	1987 Budget Request
Research and Investigation..	Section 301	42§241	Indefinite	$293,776,000	Indefinite	$296,019,000
National Institute of Child Health and Human Development..............	Title IV, Part F	42§289d and 398f-h	Indefinite		Indefinite	
National Research Service Awards............	Section 472	42§2891-1	$244,000,000 1/	13,303,000	260,000,000 1/	13,100,000
Total Budget Authority....				307,079,000		309,119,000

1/ This training authority is shared with other research training programs of the National Institutes of Health, the Alcohol, Drug Abuse, and Mental Health Administration; and the Health Resources and Services Administration.

National Institute of Child Health and Human Development

Appropriation History

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation 1/
1978	$157,015,000	$163,890,000	$168,129,000	$166,390,000
1979	198,931,000	119,005,000	109,605,000	197,630,000
1980	204,949,000	208,981,000	204,000,000	208,953,000
1981	217,148,000	220,230,000	220,472,000	220,628,000
1982	203,362,000 2/	238,411,000	236,248,000	226,309,000
1983	233,575,000	251,561,000	255,749,000	254,318,000
1984	256,592,000	265,180,000 3/	264,847,000 3/	273,359,000
1985	280,178,000	296,929,000 4/	316,100,000	310,540,000
Rescission	-309,000			
1986	294,282,000	306,812,000 5/	323,071,000	321,796,000
1986 Sequester	-13,838,000			
1986 Proposed Rescission	-1,150,000			
1987	309,119,000			

1/ Reflects enacted supplementals, rescissions, and reappropriations.

2/ Reflects the September amendment; the original request was $231,093,000.

3/ Excludes $9,297,000 in NRSA training programs not considered.

4/ Excludes $9,831,000 in NRSA training programs not considered.

5/ Excludes $13,901,000 in NRSA training programs not considered.

National Institute of Child Health and Human Development

Justification

	1986 Appropriation Amount	1986 Available after sequestering Amount	1986 Revised FTEs	1986 Revised Amount	1987 FTEs	1987 Amount
Research for mothers and children	$165,489,000	$157,972,000	—	$157,272,000	--	$156,959,000
Population	105,923,000	101,790,000	—	101,340,000	--	101,428,000
Intramural research	35,733,000	33,981,000	255	33,981,000	255	35,746,000
Research management and support	15,137,000	14,486,000	164	14,486,000	164	14,986,000
Total	322,282,000	308,229,000	419	307,079,000	419	309,119,000

General Statement

The National Institute of Child Health and Human Development (NICHD) has one of the broadest research missions of any of the Institutes at the National Institutes of Health. Its research programs are aimed at developing a solid basic science base in the biomedical and behavioral sciences to provide the foundation for understanding fundamental, universal processes such as sexual maturation and fertility, reproduction, pregnancy, and infant, child and adolescent development.

There are many processes involved in the successful achievement of each of these developmental steps in the life cycle, and thus, there are many opportunities for problems to arise. Because each of these steps is so fundamental to the development of a healthy, functional adult, problems that arise during any of the maturational processes can result in some of the most devastating and costly health problems facing our Nation. These include infant mortality, mental retardation, genetic defects, unwanted or unintended pregnancies, learning disorders, and infertility.

The research philosophy of the NICHD is that through understanding normal development, scientists will be able to develop strategies, treatments or therapies to ameliorate or, better yet, to prevent problems from arising.

To meet this goal, the NICHD supports through grants and contracts and conducts in its own laboratories a broad range of biomedical and behavioral research. The Institute is divided into three major divisions: The Center for Research for Mothers and Children (CRMC), which studies issues such as prematurity, infant mortality, high risk pregnancy, mental retardation, and human learning and behavior; the Center for Population Research (CPR), which studies fertility and infertility, contraception, and population issues; and the Intramural Research Program (IRP), which focuses on issues relevant to both the health of mothers and children and population research. A fourth component of the NICHD, the Epidemiology and Biometry Research Program, conducts and supports research on the incidence and prevalence of problems such as low birth weight and which identifies risk factors for various disorders.

Overall Budget Policy

The budget request is $309,119,000, which represents an increase of $2,040,000 over the 1986 revised estimate. Of the total amount available in 1987, some 61 percent, or $189,631,000, is for the support of 1,369 research project grants. These levels will be achieved by limiting indirect cost and by negotiating direct costs downward. The request will support 456 competing project grants at an average cost of $137,776. This represents essentially the same level of direct costs as 1986 and a 9.8 percent reduction from full recommended levels. Historically, these reductions have averaged 3 percent. The request will support 913 noncompeting project grants at an average cost of $137,421. This represents essentially the same level of direct costs as 1986 and a 9.6 percent reduction from full commitment levels. Historically, these reductions have averaged 1 percent.

The request will allow the Institute to fund 43 research center grants, at $26,217,000, the same number, and at essentially the same average cost, as in 1986. This represents a 16 percent reduction from full recommended or committed levels in 1987; in 1986, the reduction averaged 12 percent.

The budget reflects a decrease of $203,000 and 11 full-time National Research Service Award training positions, as compared with 1986. NICHD research and development contracts will be funded at the same level, $22,156,000, and at the same average cost as in 1986.

There is an increase of $1,765,000 for the Institute's intramural research program. Among the highest priorities of the NICHD are intramural projects in immunology and in vaccine development. Over 50 percent of the increase is attributable to mandatory cost increases. In Research management and support, the increase of $500,000 over 1986 is exclusively for mandatory costs.

The request excludes $700,000 for AIDS research in 1987, which is under the single AIDS appropriation in the Office of the Assistant Secretary for Health.

Program Accomplishments

NICHD-supported scientists have isolated and characterized a protein that appears to block a hormonal step necessary for the development of sperm and egg cells. Because the protein, called inhibin, blocks this step without upsetting the body's hormone balance, it may lead to improved birth control pills for women and provide the basis for a hormone contraceptive for men.

A team of NICHD intramural scientists have determined the structure of the gene encoding the cellular receptor for interleukin-2 (IL-2), an essential chemical of the immune system that helps infection-fighting cells multiply. By studying immune cells, called T cells, taken from patients with a rare, virus-caused leukemia, the researchers found an abnormality that may explain why these cells grow uncontrollably. This finding may lead to a better understanding of this form of leukemia.

Other intramural scientists have discovered that an embryo's first proteins form the "bones" of a cell. These thread-like proteins, called cytokeratins, run through the cell's interior helping the cell keep its shape. Because cytokeratins arise in embryonic cells destined to become skin, this tissue appears to be among the first to specialize during development. Cytokeratins are produced only during the embryonic period. Identifying genes and proteins active only in the embryo will facilitate the search for unique molecular signals that control embryo development. Understanding these signals would be an important step forward in identifying the causes and discovering treatments or methods to prevent birth defects.

By the end of the next decade, DNA segments representing the complete set of human genes may reside in a repository located in Rockville, Maryland. The repository will be a central warehouse where copies of human DNA segments, called probes, can be collected, stored, and distributed to scientists around the world. DNA probes are valuable molecular tools for genetic researchers to locate genes on specific chromosomes, reproduce identical gene copies, and distinguish normal from abnormal genes. Established and funded by the NICHD, the repository will enable scientists to locate and easily acquire small pieces of human DNA to study and diagnose genetic diseases.

Over the past year, NICHD-supported researchers have reported major findings about three leading methods of birth control: oral contraceptives, intrauterine devices (IUDs), and spermicides. Some of the results were good news for consumers; others were not.

Among the good news, a group of NICHD-supported researchers reported that young women who have used oral contraceptives are at no greater risk of developing breast cancer than are women who have never used birth control pills. Previously, concern had been raised about the possibility of pill use leading to an increased rate of breast cancer in young women. This study, the first to look specfically at the relationship between oral contraceptive use and breast cancer that develops at an early age, appears to lay those fears to rest. The study found that regardless of the age at which women started using the pill or how long they used it, there was no increased risk of breast cancer in premenopausal women. The researchers are now looking at older women (post-menopausal) to determine if pill use affects their risk of breast cancer. In the U.S., the birth control pill is the second most popular method of contraception, next to sterilization. About 70 percent of all women have pled birth control pills at some time during their reproductive years.

Also, there was reassuring news for women who use contraceptive spermicides. Research reported by NICHD epidemiologists shows that women who use contraceptive spermicides and unintentionally become pregnant have no greater chance of producing a premature or low birth weight infant or an infant with a birth defect than do women who become pregnant while using other types of contraceptives. Several recent, smaller studies had suggested that spermicide use around the time of conception may be harmful to the fetus, but those findings are refuted by this large, well-designed NICHD study. Spermicides, such as contraceptive jellies, creams, and foams, contain chemicals that prevent pregnancy by damaging the sperm. About 10 percent of U.S. women use spermicides to prevent pregnancy, and about 15 percent of women who use spermicides still become pregnant. Some women continue to use spermicides after conception because they are unaware that they are pregnant, so any association between their use and effects on the fetus would have major public health implications.

NICHD-supported research raised some concern about the safety of some IUDs. Two studies have found that women who have used IUDs for birth control are more likely than other women to become infertile. This increased risk seems, however, to depend largely on the type of IUD used. These findings are the first direct evidence of a long-suspected link between the IUD and infertility. An estimated 2.2 million women in the U.S. use the IUD. The studies indicate that the copper-bearing devices, the most popular type of IUD in use today, are less likely than other IUDs to lead to infertility. The researchers estimate that IUDs may account for infertility in some 88,000 women in the U.S.

The deleterious effects of smoking on pregnancy have been well documented. There has long been evidence that smoking during pregnancy, on average, reduces the birth weight of the newborn by about 7 ounces. Now a new NICHD-supported study has evidence that smoking is also a factor in prematurity. In a study of more than 36,000 women, it was found that pregnant smokers were 20 percent more likely to deliver more than 3 weeks early. Even more critical is the finding that women who smoked one or more packs of cigarettes a day were 60 percent more likely to deliver 8 or more weeks early, compared to non-smokers. It was found that the number of babies born 8 or more weeks early would decrease by 8 percent if all pregnant women were to quit smoking. Since a large portion of the Nation's infant mortality occurs among very preterm infants, maternal smoking during pregnancy appears to be a significant factor in this Nation's relatively high infant mortality rate.

The incidence of ectopic pregnancy in the U.S. has more than doubled in the past decade. Ectopic pregnancy almost always results in the death of the fetus and is a life-threatening situation for the mother as well. A team of investigators supported by the NICHD has discovered a probable cause to account for at least some of this increase: vaginal douching. In a recently reported study, it was found that women who use a commercial douche at least once a week were more than four times as likely as women who never douche to have an ectopic pregnancy. It was also found that vaginal douching may increase the risk of pelvic inflammatory disease which is known to predispose women to ectopic pregnancies and infertility.

NICHD participated in clinical trials which led to the FDA's approval in October of 1985, of synthetic growth hormone. Previously human growth hormone was available only from the pituitary glands of cadavers. This supply was inadequate to treat the hundreds of thousands of children in this country who are extremely short for their age. Now that synthetic growth hormone has been approved for marketing, there will be a supply sufficient to meet the needs of these children and there will also be increased availability of the substance for research purposes.

Recent studies by two NICHD grantees have shown that injections of synthetic growth hormone produce growth acceleration in short children who are not deficient in human growth hormone, as well as in short children who do have a deficiency. Since some growth deficient children produce adequate quantities of growth hormone but are short for genetic, constitutional or unknown reasons, the finding that synthetic growth hormone will accelerate their growth means that many more children will be able to reach a normal size.

In response to fears that were raised concerning a possible association between Sudden Infant Death Syndrome (SIDS) and DPT vaccinations, NICHD epidemiologists analyzed data from a large U.S. multicenter, case-control study and found no association between the two. In fact, SIDS victims were less likely than the living controls to have received any DPT vaccination.

NICHD-supported scientists have developed a reliable test to detect pregnancy at its earliest stage. The test depends upon measurement of a hormone produced by the embryo. Using this test, it has been found that in a general population of normal women, the fetal loss rate may be as high as 50 percent, with the losses coming so early that most of the women would not have realized that they were pregnant. Until now, there has been no way to assess how common early pregnancy loss is, nor in which women it occurs. Since repeated early pregnancy loss may be an unrecognized cause of infertility in some women, this test will be a useful clinical tool.

An NICHD intramural researcher has developed a computer program that can be used by diabetic adolescents for the self-management of their disease. This development is important because diabetes is a very common illness; treatment in young patients often must be adjusted daily; and most adolescents rebel against this tight regimen. By giving the young patient control over his own treatment, and by taking advantage of the popularity of home computers, control of diabetes in adolescents has been facilitated.

In immunological applications of new biochemical and molecular methods, NICHD intramural scientists have recently isolated, purified and characterized the toxin of the pertussis organism (the bacteria which causes whooping cough), and have initiated field trials of the detoxified toxin which they believe will form a much safer and more effective pertussis vaccine than the DPT inoculations currently administered.

In other work, these same intramural scientists have been successful in generating new vaccines against typhoid fever and *Hemophilus influenzae* type B. While there has been a typhoid vaccine available for many years, the side effects and short-lived immunity associated with this vaccine have precluded wide acceptance. The new vaccine, which is now in field trials in India and Nepal, appears to avoid these pitfalls. *Hemophilus influenzae* is a serious cause of sickness and death in infants, despite effective antibiotics and the availability of a recently licensed vaccine that is effective in older children. The NICHD vaccine fully protects infant monkeys and is very promising for use in humans.

AIDS Research Program

The request does not include support for AIDS research. However, AIDS does relate to NICHD program interests in the areas of reproductive health, sexually transmitted diseases, maternal transmission of AIDS to offspring during pregnancy and the neonatal period, development of the child infected in utero with the AIDS virus, and non-medical care of the infant or child with AIDS.

NICHD staff have developed several proposals which have been submitted to NIH for consideration by the AIDS Executive Committee. These proposals, if approved for support in FY 1987 would be provided from funds made available to the Director, NIH. Included among these proposals are:

1. Role of Barrier Contraception in Prevention of AIDS Transmission. Barrier contraception may prevent the transmission of HTLV-III within high-risk AIDS populations. The efficacy of various combinations of barrier contraceptives to reduce the risk of AIDS should be evaluated so that firm contraceptive-use recommendations can be made for current high-risk populations. These findings will be generalizable for the population-at-large.

2. Effect of HTLV-III Infection on Pregnancy. The majority of children with AIDS are the offspring of mothers who have the syndrome themselves, who belong to high risk groups or who are sexual partners of members of high risk groups. However, the actual route of transmission in these cases is presently unknown. The NICHD is currently collaborating with the NCI in a study of pregnant women who are members of groups at risk for AIDS. The protocol has been designed and subject recruitment mechanisms are in place. It is the primary goal of this study to assess the rate and mode of HTLV-III transmission as well as the outcome of the children who become infected with the virus.

3. The Clinical Spectrum of Disease in Infants. To date, a description of the clinical spectrum of HTLV-III disease in children has relied on unsystematic investigation and reporting based upon relatively small numbers of cases. Preliminary evidence suggests that an as yet unquantitated proportion of infants born to HTLV-III positive women will develop AIDS. It has been demonstrated that some children with AIDS or probable AIDS suffer from low birth weight, failure to thrive and, in some cases, striking developmental and neurologic impairment (Ped Res 19: 395A, 1985). However, the clinical course and growth and development of infants and children who have asymptomatic HTLV-III infection or lesser AIDS is unknown. The current NCI-NICHD study provides an opportunity to address these questions. The NICHD proposes to supplement and expand the investigations currently planned to include systematic pediatric neurologic assessment of affected children and provision of a network of pathologists, immunologists, virologists and oncologists to process and examine pathologic specimens.

National Institute of Child Health and Human Development

Research for Mothers and Children

1987 Authorization: Indefinite.

Budget Authority:

1986 Appropriation	1986 Available after sequestering	1986 Revised Estimate	1987	Increase or decrease
$165,489,000	$157,972,000	$157,272,000	$156,959,000	-$313,000

Purpose and Method of Operations

Since 1962, the National Institute of Child Health and Human Development (NICHD) has dedicated itself to studying ways to improve the health of mothers and children. It supports and conducts research directed toward ensuring the optimal outcome of pregnancy and toward maximizing the health potential of the 3.7 million infants born in the U.S. each year.

The Center for Research for Mothers and Children (CRMC) is the primary extramural program supporting research on maternal and child health at the NICHD and at the National Institutes of Health. CRMC research encompasses areas such as: fetal development, pregnancy and birth, infant mortality and morbidity, the role of nutrients and hormones in growth and development, the causes and prevention of mental retardation, and the learning and cognitive processes involved in behavioral development.

Two-thirds of all infant deaths occur among low birth weight infants. With today's improved neonatal intensive care, most infants of 1,500 to 2,500 grams survive and do fairly well but infants born weighing less than 1,500 grams do not fare as well. These infants require long periods of intensive care and some have life-long residual effects. Low birth weight may be due to intrauterine growth retardation, premature labor, or both.

Rationale for the Budget Request

The 1987 request is $156,959,000, a decrease of $313,000 below the 1986 estimate. The following are the program plans for 1987.

LOW BIRTH WEIGHT

In 1984, the NICHD began a major special initiative: an expanded research program in the prevention of low birth weight. Low birth weight is the most important problem in maternal and child health in the U.S. today.

The low birth weight initiative includes stepped-up research efforts in intrauterine growth retardation (IUGR) and fetal growth and in prevention of premature labor. As part of its initiative, the NICHD recently funded two large projects in response to a Request for Applications in the area of intrauterine growth retardation. One of the multi-project grants is targeted at understanding the mechanisms of fetal and neonatal growth, elucidating the effects of growth hormone, nerve growth factor and other substrates on fetal growth; and probing the dynamics of uterine and umbilical blood flow. The other is focused on basic and clinical research on the physiology of IUGR in animal models with the long term goal of decreasing the incidence of fetal and infant deaths and improving the quality of life of surviving infants with IUGR.

PRETERM LABOR AND BIRTH

Prematurity is a major cause of low birth weight. The possibility that certain bacterial infections might contribute to the high rate of prematurity and resultant low birth weight in the U.S. is under active investigation. A small study was recently completed which detected a relationship between cervical inflammation and preterm delivery. A large follow-up study is now under way in which more than 10,000 pregnant women will be examined for vaginal infections. Women with certain types of infections will be treated with antibiotics to see if this therapy reduces the risk of prematurity. Results from this study are expected in approximately two years.

Other NICHD-supported investigators are studying uterine muscle activity during gestation in sheep and rhesus monkeys in order to understand better the transition from non-labor "contractures" to the "contractions" associated with labor and birth. Other research is characterizing a substance found in amniotic fluid which is apparently a fetal "signal" to initiate labor. Still another scientist is evaluating in animal models to ascertain the potential fetal side-effects of pharmacologic agents now used to arrest preterm labor in humans.

DISORDERS OF THE NEWBORN

The utilization of many drugs and therapeutic modalities for sick newborns in neonatal intensive care units is being surveyed in-depth by an NICHD-supported team of researchers. They have identified substantial changes in daily practices, documented significant exposures of very sick infants to various pharmaceutical additives causing serious reactions, and suggested a relationship between the routine use of a drug (heparin) and an increase in the risk of hemorrhage in the brain. Further studies in this area will be important to delineate appropriate treatment regimens in this age group.

The potential of diagnostic ultrasound to assess the status of fetal lung maturity is being evaluated as an attractive alternative to direct biochemical analysis of amniotic fluid. Such improved technology would facilitate and improve perinatal management directed at the prevention of respiratory distress syndrome (RDS) in newborns. RDS is the most common cause of death among premature infants.

SUDDEN INFANT DEATH SYNDROME (SIDS)

NICHD has the primary Federal responsibility for research on Sudden Infant Death Syndrome (SIDS). The program objectives are to clarify the cause(s) of the syndrome, to identify infants at risk, and to explore approaches to prevent SIDS. A Request for Applications has been issued to stimulate further research in these areas with special emphasis on the possibility of identifying abnormalities in the central nervous system and brainstem of those infants.

Next September, the NICHD will sponsor a consensus development conference on Infant Apnea and Home Monitors. Materials presented at this meeting should clarify the relationship, if any, between apnea and SIDS, and determine whether home apnea monitors are useful in preventing SIDS.

ENDOCRINOLOGY, NUTRITION, AND GROWTH

Neuropeptides and Cerebral Control of Growth and Development - A major biomedical research challenge is to elucidate the functions of the growing number of neuropeptide hormones that are being discovered in the brain, including various polypeptides usually associated with digestion and nutrient metabolism, such as cholecystokinin and insulin. These and other neuropeptides are becoming increasingly recognized as controlling many aspects of growth and development, including body size, body composition, appetite, obesity, puberty and fertility. The Institute is supporting research on the neuroendocrine control of growth during fetal life, infancy, childhood and adolescence. These studies should enhance our understanding of the neuroendocrine aspects of growth retardation in utero and during childhood.

Infant Nutrition - In the area of nutrition, the Institute is responding to a number of challenges, the most urgent of which is to determine the nutrient requirements for very low birth weight infants and to devise methods of optimal nutritional support for them. Some fortified mothers' milk has for example, failed to provide enough phosphorus for rapidly growing bones. There is a pressing need to place the nutritional management of these fragile newborns on a more reliable scientific basis. Research proposals funded in FY 1986 will explore the composition and beneficial properties of human milk, including its protective immunologic components; and the digestive enzymes present in milk that supplement the newborn's own digestive function.

One recent observation that is highly important to the infant feeding issue relates to AIDS. Because human milk is a body secretion, the AIDS virus may be transmitted to infants during feeding. In fact, the AIDS virus and antibody to it have been identified in milk. Other viruses have also been identified in fresh human milk; however, these viruses often confer immunity to infants receiving their mothers' milk. Whether this beneficial effect will occur with milk infected with AIDS virus is not known.

GENETICS AND TERATOLOGY

Limb Malformations - Developmental defects of the limb remain a major research focus since at least 1 out of 200 newborn infants is afflicted with these deformities. The NICHD supports a sizeable research program in the area of limb malformation. This program includes research in anomalies of cartilage, muscle, and bone. Studies of the developmental disruptions resulting in markedly shortened and distorted limbs remain an area of special research interest. New information on the clinical and radiological aspects, genetic heterogeneity, biochemistry and molecular genetics of the known as well as newly discovered syndromes has resulted.

Congenital Defects - Aberrations in Early Development - Mental and physical defects resulting from faulty development remain the leading cause of death under one year of age. The concern of NICHD with prevention of these congenital defects has resulted in a special emphasis on studies of early embryogenesis and the genetic controls involved. A conference was held in April 1985 focusing on the genetic controls of the orderly development of the fertilized egg into the diverse differentiated cells and tissues of the mature organism. Genes which regulate developmental changes and genes which are themselves differentially regulated throughout development need to be identified and studied. These research areas and those requiring the discovery of new technologic or new model systems for further advancements in understanding are being emphasized. Of great importance will be the construction of sets of DNA probes that represent those genes that are active in an embryo at one specific time and in one specific tissue during early development. Such studies will provide information that is essential for understanding the processes of normal development in the human embryo, as well as congenital malformations.

MENTAL RETARDATION AND DEVELOPMENTAL DISABILITIES

Down Syndrome (Trisomy 21) - Down syndrome is the most common genetic disorder detected in infancy and serves as a model for studying nondisjunction. Nondisjunction is a genetic mechanism characterized by the failure of a pair of chromosomes to separate during cell division. In order to understand nondisjunction, the properties of chromosomes relevant to their segregation must be thoroughly researched. Biologic systems and tools to do this are now at hand in the form of DNA probes derived from chromosome 21. These are ideal genetic markers that can be regionally mapped to the chromosome. NICHD-supported investigators in several studies are applying these techniques to Down syndrome. The interrelation between nondisjunction, cross-over and maternal age should soon be uncovered by studies of this sort.

Intergenerational Effects - It has been hypothesized that "familial" retardation and other intellectual-learning disorders of unknown etiology are the products of nongenetic intergenerational effects. NICHD-supported studies in rats have shown that maternal diets low in protein produce debilitating effects that are carried over successive generations. Other studies have demonstrated that the effects of drugs, stress, and different forms of handling in infancy also are intergenerational. The NICHD will continue to try to identify specific nongenetic intergenerational influences and will examine the magnitude and duration of these effects.

Behavioral Teratology - The full ramifications of prenatal damage cannot be detected by examining the unborn and newborn for structural abnormalities. It is increasingly clear that many forms of damage to the embryo and fetus can only be detected postnatally through the detailed examination of the functional integrity of the organism. It has been shown that chemical and environmental agents capable of producing structural malformations of the central nervous system at high doses can reliably induce behavioral abnormalities at lower, non-malforming doses. Expanded research in behavioral teratology is being conducted to explore these effects across a wide range of teratological agents.

Identification of Infants at Risk for Mental Retardation - Each year thousands of premature or low birth weight infants spend the first days or weeks of their lives in neonatal intensive care units where technological and medical advances permit the survival of many critically ill infants. However, some of these survivors will be mentally retarded or developmentally disabled by the time they enter elementary school. Early determination of which infants are at risk for developmental disabilities may allow for early behavioral and educational intervention to try to prevent or ameliorate mental retardation. Continued research and development on these issues will permit optimal and efficient intervention strategies to be established.

Research on Families With Mentally Retarded Children - Recent efforts to find alternatives to institutionalization have resulted in larger numbers of retarded children remaining with their families. The abilities of families to facilitate the growth and development of their retarded youngsters are only beginning to be understood. New behavioral research techniques are now available which make it possible to study the ways in which retarded children enrich their families as well as the ways families are adversely affected by the stress of having a retarded child. Further research is being conducted on families with mentally retarded children in order to develop information to help parents and communities integrate these children and adults into the mainstream of modern American life.

HUMAN LEARNING AND BEHAVIOR

This program supports basic research and research training on behavioral development from the perinatal period to the beginning of adulthood. The primary focus of the research is to determine the biobehavioral factors that underpin normal behavioral development and to identify those factors that interfere with such development.

Behavioral Pediatrics - Behavioral pediatrics is an emerging field of research that integrates the behavioral and biological sciences to study children's health behavior. Major foci include studies of health promotion, illness behavior and risk-taking and compliance behaviors in children. One of the major priorities of this program area is to gain an understanding of the behaviors that underlie unintentional injuries (the leading cause of mortality and morbidity in children) and to devise research-based procedures for preventing such accidents. A Request for Applications has been issued for this area in an attempt to stimulate increased research activity.

Developmental Behavioral Biology - Research in the area of developmental behavioral biology is devoted to studying the contributions of an individual's biological heritage to behavioral development. Advances made in understanding the relationship between brain development and behavior during the perinatal period suggest that continued support for such research should yield important new information of how mother and offspring interactions, along with environmental stimulation, help the infant successfully adapt to its surroundings.

Learning and Perception - The Institute supports a wide variety of studies on learning and cognitive development that are focused upon gaining a basic understanding of how higher mental processes evolve. Research in the coming year will focus upon studies of the neural circuitry that underlies perception and cognition. This work will lay the groundwork for understanding learning disabilities.

Communication - The NICHD sponsors a broad range of research to gain an understanding of the basic processes, both behavioral and biological, that underlie the development of speech and language in children. NICHD-supported researchers have discovered biologic markers that may make it possible to sub-type children with dyslexia (the inability to read). This finding may help clinicians devise more effective intervention strategies for dyslexic children.

Social and Affective Development - The Institute's program in social and affective development includes research on temperament, social behavior, aggression, and social cognition. These aspects of the child's development are studied in such settings as the family, peer groups, schools and the larger community. A major research focus of the program centers on the role of the family in the child's social and emotional development. A particular emphasis will be on trying to gain an understanding of such development against the background of changes in the American family such as divorce, single parent head-of-household, and delayed childbearing trends.

Impact Data	1986 Appropriation	1986 Available after sequestering	1986 Revised estimate	1987
Budget Mechanism				
Research Projects grants				
Number	814	814	804	811
Amount	128,898,000	123,070,000	122,370,000	122,268,000
Research Centers				
Number	19	19	19	19
Amount	13,973,000	13,373,000	13,373,000	13,303,000
Other Research				
Number	85	81	81	81
Amount	5,395,000	5,045,000	5,045,000	5,045,000

Training				
Number	475	455	455	448
Amount	9,786,000	9,364,000	9,364,000	9,223,000
R&D Contracts				
Number	40	39	39	39
Amount	7,437,000	7,120,000	7,120,000	7,120,000
Total				
Amount	165,489,000	157,972,000	157,272,000	156,959,000

National Institute of Child Health and Human Development

Population

1987 Authorization: Indefinite.

Budget Authority:

1986 Appropriation	1986 Available after sequestering	1986 Revised Estimate	1987	Increase or decrease
$105,923,000	$101,790,000	$101,340,000	$101,428,000	+$88,000

Purpose and Method of Operations

The NICHD Center for Population Research (CPR) is responsible for the primary Federal research program in the areas of reproductive biology, population dynamics and contraceptive development and evaluation. Fundamental biomedical research in the reproductive sciences relevant to the problems of human fertility and infertility is emphasized. This research provides the bases for the development of safe and efficacious methods for fertility regulation and the evaluation of the benefits and risks of current contraceptive methods. Demographic and behavioral sciences research on the causes and consequences of population structure and change is also supported. Funding is provided through grants and contracts and includes the support of population research centers and research training.

Rationale for the Budget Request

The 1987 request is $101,428,000, an increase of $88,000 over the 1986 level. The following are the program plans for 1987.

REPRODUCTIVE SCIENCES

The major emphasis of the Institute's reproductive sciences program is to maintain a basic science research base in reproductive medicine, endocrinology, genetics and immunology, and in the developmental biology of reproduction and embryonic development. This base facilitates efforts to alleviate human infertility; ameliorate or cure human reproductive diseases and disorders; understand the development of healthy embryos; and to discover new leads for the development of safe, efficacious, and widely acceptable methods of fertility regulation.

The Institute's research program in the reproductive sciences encompasses reproductive medicine, including studies for the treatment of infertility in women and men, studies for the alleviation of human reproductive diseases and disorders, studies for the precise monitoring and effective prevention of ectopic implantation of embryos and pregnancy wastage, and studies concerning the relationship of pelvic inflammatory disease to reproductive failure. Reproductive endocrinology, including studies on the structure and the synthesis of reproductive hormones, of the regulation of gene expression by sex steroid hormones, and of the endocrine signals that are involved in reproductive disease and health, is a major component of the program. Research is also supported in reproductive genetics and immunology. This includes studies of the genetic basis of reproductive disorders and studies to detect or quantitate reproductive hormones or reproductive tract tissue secretions important in the diagnosis of reproductive disorders and the evaluation of therapeutic efficacy. An exciting new area of research is exploration of the potential for fertility regulation by immunologic methods, and studies of the immunologic factors associated with infertility.

CONTRACEPTIVE DEVELOPMENT

The NICHD program in contraceptive development supports clinical trials and laboratory studies that are aimed at developing improved methods of fertility regulation for both men and women which are safe, effective, reversible, and acceptable to the public. This involves the development of new drugs to regulate fertility in both sexes; the development of improved methods of drug administration; and the improvement of barrier methods of contraception.

Several clinical trials in the area of contraceptive development are under way. These include studies of synthetic analogs (copies) of the brain hormone, luteinizing hormone releasing hormone (LHRH), for fertility regulation in men and women; studies evaluating long-acting implants and injectables; and studies exploring new steroid combinations for male contraception. Research seeking improved barrier methods, including the cervical cap and new variations of the diaphragm, is under way, and the testing of new oral contraceptives continues.

CONTRACEPTIVE EVALUATION

The NICHD program in contraceptive evaluation, in accordance with its objective of furthering research on the safety and efficacy of current methods of contraception, supports clinical trials, large health surveillance cohort studies, and prospective and retrospective epidemiological studies that seek to quantify the risks and benefits associated with the use of oral contraceptives, intrauterine devices, barrier methods, and sterilization procedures.

Data from the second National Health and Nutrition Examination Survey, compiled by the National Center for Health Statistics, have been analyzed under an NICHD-supported interagency agreement, to assess the cardiovascular risk profile of oral contraceptive (OC) users and nonusers in the United States. The data indicate that 8 percent of U.S. women who use OCs have three or more established risk factors for atherosclerotic heart disease, such as smoking, elevated total cholesterol, or obesity, while they are users of contraceptive pills. In addition, it has been shown that more than 45 percent of OC users have at least one risk factor for heart disease and that the most common risk factor for heart disease in OC users is smoking.

As part of the NICHD research program in contraceptive evaluation, scientists are continuing to try to determine if there is an association between reproductive system cancer and long term exposure to currently marketed contraceptive steroids. They also are studying the physiologic and metabolic changes that occur in oral contraceptive users, and evaluating the benefits of contraceptive steroids such as their protective effects against certain diseases, including specific types of cancer. Intrauterine devices (IUDs), are also being studied, focusing on their role in the occurrence of undesired infertility, the mechanisms by which IUDs may contribute to pelvic inflammatory disease, and how various infectious agents enter the IUD-containing uterus. Because both male and female sterilization surgery continues to be a popular family planning choice, the NICHD is supporting studies on its long-term health effects and the failure rates of various procedures used for female sterilization. Other ongoing research includes studies to ascertain and quantify the reduction in the risk of venereal disease and pelvic inflammatory disease among women who use barrier methods of contraception; to evaluate the use-effectiveness of barrier methods, including the new contraceptive sponge; and to estimate the role of barrier methods in the genesis of newly documented gynecological disorders, such as toxic shock syndrome.

DEMOGRAPHIC AND BEHAVIORAL SCIENCES

The Institute's program of research in the demographic and behavioral sciences focuses on the size, rate of growth, and composition of our nation's population and the impact of population change on the health and well-being of individuals, families, and society as a whole. This involves studies on the causes and consequences of the three components of population change: fertility, migration, and mortality.

An NICHD-supported study has been assessing the effects of teen parenthood on the offspring's school-related achievements. The most important predictor of the child's academic progress was found to be the mother's own educational attainment. The higher the level of schooling of the mother, the better her child tended to be in both vocabulary score and grade progression. Children of mothers who were in school at the time of pregnancy or who dropped out and returned to complete additional schooling, did much better than the children of mothers who had dropped out of school permanently. Even among children of women who delayed childbearing past the high school years, the children of mothers who dropped out of high school were found to have lower vocabulary scores.

Other research in the demographic and behavioral sciences supported by the NICHD includes identifying and analyzing trends in fertility by social and economic characteristics and identifying the interacting factors between fertility and family planning which contribute to effective fertility regulation. Studies on family and household structure, including the effects of family structure on child health and development, and on the status and roles of women, including the interrelationships between women's status, roles as wife, mother and labor-force participant, and the number, spacing and timing of births are also supported. Other issues such as child care and fertility, including studies of how costs and availability of child care influence decisions regarding employment and childbearing, and the cost and value of children, including the extent to which men and women with varying characteristics evaluate the costs and benefits for various numbers of children and the timing of births, also are supported by the NICHD. The Institute also supports some research in migration such as the relationship of immigration to health status and fertility.

Impact Data	1986 Appropriation	1986 Available after sequestering	1986 Revised estimate	1987
Budget Mechanism				
Research Project grants				
Number	560	560	554	558
Amount	70,313,000	67,595,000	67,145,000	67,363,000
Research Centers				
Number	24	24	24	24
Amount	13,565,000	12,982,000	12,982,000	12,914,000
Other Research				
Number	33	32	32	32
Amount	2,215,000	2,238,000	2,238,000	2,238,000
Training				
Number	199	190	190	186
Amount	4,115,000	3,939,000	3,939,000	3,877,000
R&D Contracts				
Number	69	67	67	67
Amount	15,715,000	15,036,000	15,036,000	15,036,000
Total				
Amount	105,923,000	101,790,900	101,340,000	101,428,000

National Institute of Child Health and Human Development

Intramural Research

1987 Authorization: Indefinite.

Budget Authority:

1986 Appropriation	1986 Available after sequestering	1986 Revised Estimate	1987	Increase or decrease
$35,733,000	$33,981,000	$33,981,000	$35,746,000	+$1,765,000
		(FTEs: 255)	(255)	(--)

Purpose and Method of Operations

The Intramural Research Program of the NICHD is staffed by scientists who conduct research on the biomedical and behavioral aspects of human development. This research includes studies on reproduction and on maternal and child health, as well as epidemiologic investigation in areas of high priority to the Institute. The program emphasizes studies in animals that serve as models for human development, as well as studies in humans of genetic diseases and inborn errors of metabolism, congenital malformations, and endocrine and metabolic disturbances.

Rationale for the Budget Request

The 1987 request is $35,746,000, an increase of $1,765,000 over the 1986 estimate. The increase reflects an additional $766,000 for mandatory cost increases, and a program increase of $999,000. The following are the program plans for 1987.

Laboratory and Clinical Research - This program is broadly concerned with the biological and neurobiological, medical and behavioral aspects of normal and abnormal human development. The program's goal is to probe deeply into all of the life processes as a basis for maintaining health, as well as for the prevention and treatment of disease. This goal reflects the belief that the key to the prevention of common "adult" diseases, such as cancer, heart disease, mental illness, and premature aging, lies in our understanding of the rules which govern early development. Research is carried out in patients as well as in a diversity of animal models, including fruit flies, squid, frogs, mice and primates. Currently, two areas of investigation are being emphasized throughout the program: intensive studies regarding the structure of genes and the regulation of gene expression knowledge in this area is critical as we embark upon an era of "gene therapy," and studies of "signal transduction," the complex neurotransmitters, antigens, carcinogens, and drugs).

A major effort is devoted to studying the causes and treatment of infertility. Intramural scientists are testing synthetic analogs of an important brain hormone (LHRH) which may greatly promote or reduce fertility in women depending on the dose and type of analog. The ability to suppress or augment hormonally mediated events with synthetic preparations of LHRH has also been used with excellent results in some patients with breast and prostate cancer, and in children with the premature onset of puberty. With respect to male infertility, specific proteins have recently been identified which coat the head of the sperm and serve as a recognition site for the sperm-egg interaction. In a high proportion of men with infertility of unknown origin, NICHD scientists have found that these proteins are qualitatively or quantitatively abnormal, suggesting that it may be possible to design an immunological therapy for this disorder.

The critical events which determine normal or abnormal development occur very early during embryogenesis. In basic studies on birth defects, NICHD scientists are studying the molecular processes involved in the transmission of genetic information from parent to child, and the expression of this information as the organism develops from a single cell to a complex individual. Using the recombinant DNA techniques of biotechnology, it is now possible to examine how genes code for individual body parts, such as a limb or an organ, and how defects in these genes lead to congenital malformations. Fortunately, these genetic pathways appear to be very similar between humans and such easily studied animals as fruit flies. NICHD scientists have recently identified and cloned an important gene ("fs-l-h") that determines whether the body segments in the fruit fly arise normally, e.g., the antennae from the head and the wings from the thorax. They have found, in fact, that the gene must be abnormal both in the mother and in the embryo before a birth defect appears. It is likely that studies in simple animals will lead to the discovery of "universal markers" for congenital defects that can be used to diagnose and possibly correct some human abnormalities prenatally. Using another animal model, the frog, intramural scientists have recently identified the earliest genes to be expressed in the fertilized egg. These genes appear to be "turned on" after only three or four cell divisions, and it is probable that the products of these genes determine all further development. NICHD scientists are now studying the factors that turn on these genes, such as cell-cell interactions in the embryo or factors transmitted in the egg. The products of these very important genes have been identified and purified, and the genes themselves have been cloned. This frog model will permit a major increase in our understanding of the genetic mechanisms that control the very earliest stages of human development.

Intramural biologists are also studying the new technique of gene transfer, in which animal genes are cloned in bacteria and later inserted into the eggs of mammals; the eggs are fertilized in vitro and then transferred into surrogate mothers. These scientists have found recently that the transferred genes are stably inherited through many generations. Moreover, the genes are turned on only in the "correct" tissue at the "correct" time in development, e.g., while the gene that encodes the lens protein is transferred to every cell of the animal, it is only expressed in the eye. Thus, this important new method is teaching us how and why genes are expressed in different tissues and at different times, not only during development but in adults as well. The transfer technique, gene therapy, when perfected, promises to be definitive with respect to the correction of many human genetic disorders, and will have countless agricultural and industrial applications. Moreover, the transfer method can also be used to create animal models for human diseases; the inserted genes can be used to interrupt the function of normal, essential genes. Their "loss-of-function" animal models will permit us to test medical treatments for genetic disorders in animals before their introduction to patients. These studies comprise the most direct path leading from molecular biology to the prevention or cure of many important human diseases.

While the advent of "gene therapy" will eventually permit the primary correction of heritable human diseases, continuing study of the biochemical consequences of defective genes and the rational design of effective remedies are currently saving many young lives. For example, NICHD investigators are studying cystinosis, an inherited metabolic disorder in which the amino acid cystine accumulates to toxic levels, stunting growth and eventuating in lethal failure of the kidneys. The biochemical defect accounting for this disease has now been identified, and with this understanding, it was possible to design a pharmacological therapy (cysteamine) which has very dramatically arrested the disease in children treated at a sufficiently early age. Simple treatments for other genetic diseases have also been recently developed by NICHD scientists, including the use of purified growth hormone releasing factor (GRF) in children with a growth deficiency and a facile new diet which is extending the life-span of children with a usually fatal metabolic disorder, glycogen storage disease.

There is no theory of normal growth (nor of cancer) in the sense that we have a theory of evolution. However, studies in developmental biology and cancer research are presently running in parallel; this parallelism has been given particular impetus by the recent discovery of human onc genes. The normal functions of these genes appear to relate to cell growth and division, and differentiation. While many laboratories are exploring the cancer-causing role of abnormal onc genes, NICHD scientists are studying the role of these genes in normal development. Because onc genes have been highly conserved throughout evolution, it is possible to use simple models, such as yeasts, to study the central questions in modern biology posed by the discovery of onc genes, particularly with regard to normal and abnormal developmental events, the cause of cancer, and aging.

The nervous system is the most complex tissue in the body, and thus the most difficult to study. However, intramural neurobiologists have recently developed a system which permits brain cells to be cultured easily in plastic dishes, and which makes possible detailed correlations, during critical periods of brain development, between the electrical activity of these cells, the regulation of their genes by various hormones, and their interactions with other brain cells. This new in vitro system also permits an assessment at the molecular level of the influence of drugs and toxins on subtle aspects of brain development. Computer simulation methods permit easier analyses of the complex, integrated neurobiologic phenomena occurring in the tissue culture model. Coupled with our new ability to analyze the structure and expression of brain genes (using monoclonal antibodies and recombinant DNA methods), this technology will soon make possible a far-reaching study of the human genome as it influences normal and abnormal brain development. These results will help us to understand and possibly to prevent many cases of mental retardation.

Another group of NICHD neuroscientists is studying the problem of nerve growth, which is of great importance in spinal cord and brain injuries. These scientists have discovered a set of enzymes which determine the correct origin, dimensions, and length of the nerve. With this result in hand, it may be possible to manipulate nerve growth therapeutically.

Within the past few years, a new NICHD intramural research effort has been initiated on the genetics of behavioral development in a rhesus monkey model. Specially bred monkeys appear to have one of two heritable types of behavior, "uptight" and "laid back." These behaviors are distinguishable only under stress, but are detectable within hours after birth and throughout life. When uptight monkeys are stressed, they may display learning and communication disorders, depression, addictive behavior, and even autism. Adult monkeys of the uptight type, when stressed, may abuse their children. In contrast, laid back animals handle stress well. This model of human behavior thus has great importance, since the monkeys seem to display the full repertoire of normal and abnormal human behavioral development. NICHD researchers are now able to study the genetic and environmental interactions which determine behavioral development in these animals at a very sophisticated level, including that of gene expression and hormonal regulation. These scientists are also investigating whether the expression of these heritable behavior patterns can be altered through environmental maneuvers, such as the raising of uptight infant monkeys by laid back mothers, as well as early pharmacologic intervention.

Scientists in another intramural laboratory have identified a cluster of genes in mice which encode the enzymes that metabolize environmental pollutants, including drugs, carcinogens, and mutagens. They have bred genetic strains of mice which express these enzymes well or poorly, and have shown a correlation between the level of expression and the risk of cancer and birth defects. These scientists have recently been able to clone several of the mouse genes for these drug-metabolizing enzymes, and are using these genes to probe for their analogs in humans. If the same genes exist in humans and function similarly, it should be possible to develop molecular biology-based assays to determine the individual human risk of cancer or birth defects from various environmental exposures.

The application of recombinant DNA and monoclonal antibody techniques has also created a new opportunity to gain insight into the development and regulation of the immune system. These new methods are permitting NICHD scientists to establish the structural and functional bases for the immunological activities which regulate all of our interactions with foreign organisms and tissues. This knowledge will greatly improve our approach to organ transplantation, and is also demonstrating why fetuses bearing paternal tissue antigens are not rejected in pregnancy by the mother (or in rare cases, how errors in the system produce recurrent abortion.) In other immunological applications of new biochemical and molecular methods, intramural scientists have recently isolated, purified and characterized the toxin of the pertussis organism (the bacteria which causes whooping cough), and have initiated field trials of the detoxified toxin which they believe will form a much safer and more effective pertussis vaccine than the DPT inoculations currently administered. In other work, these scientists have been successful in generating new vaccines against typhoid fever and *Hemophilus influenzae* type B. While there has been a typhoid vaccine available for many years, the side effects and short-lived immunity associated with this vaccine have precluded wide acceptance. The new vaccine, now in field trial in India and Nepal, appears to avoid these pitfalls. With regard to *Hemophilus influenzae*, this bacterium remains a serious cause of morbidity and mortality in infants, despite effective antibiotics and the availability of a recently licensed vaccine that is effective in older children. The new NICHD vaccine fully protects infant monkeys and is thus very promising.

Finally, recent NICHD studies suggest strongly that the mechanism by which cells sense and respond to hormones, drugs, neurotransmitters, and even immunologic antigens, is controlled through a final common pathway. This "signal transduction" pathway involves binding of the hormone, or other molecule to cell surface receptors, followed by a cascade of enzyme activations within the cell, eventuating in the turning on or off of one or more specific genes. Receptor-mediated events comprise the mechanism by which cells are able to adjust their interactions with advantageous as well as disadvantageous molecules. As we identify the elements of the signal transduction pathway, it should become possible to define discrete targets for therapeutic intervention in a wide variety of receptor-mediated disorders, including hypertension, behavioral abnormalities, infertility, some types of cancer, metabolic diseases, and immunologic disorders such as AIDS. This work is of very high priority because it promises to open countless new opportunities for treatment in many disorders characterized by inappropriate interactions of the cell with ligands which influence the cell's growth, function and viability.

National Institute of Child Health and Human Development

Research Management and Support

1987 Authorization: Indefinite.

Budget Authority:

1986 Appropriation	1986 Available after sequestering	1986 Revised Estimate	1987	Increase or decrease
$15,137,000	$14,486,000	$14,486,000	$14,986,000	+$500,000
		(FTEs: 164)	(164)	(--)

Purpose and Method of Operation

This activity is comprised of staff and support costs related to the overall administration, direction, and coordination of the Institute. Included are a variety of managerial, scientific and administrative functions ranging from scientific review and program planning to informational services and financial management. The Office of the Director, the Office of Administrative Management, the Office of Research Reporting, the Office of Planning and Evaluation and the Office of Grants and Contracts are the administrative units where these functions are carried out. The Scientific Review Program manages and coordinates scientific merit review of the extramural grants and contracts of the Institute.

The Center for Research for Mothers and Children and the Center for Population Research provide the scientific program staff who concentrate their efforts on the scientific management of the research grants, training grants, and research contract portfolios within their specific areas.

During 1987 this activity will continue to provide for the professional leadership and technical guidance needed to select the research questions which most merit investigation; to plan, direct, and implement all programs of the Institute; and to conduct a broad program of information dissemination to scientists and the public.

Rationale for the Budget Request

The 1987 request of $14,986,000 for research management and support is an increase of $500,000 over 1986. This increase is exclusively for mandatory cost increases, such as within-grade salary increases, certain utility costs, and costs for centrally furnished services.

National Institute of Child Health and Human Development

Detail of Permanent Positions

	1985 Actual	1986 Estimate	1987 Estimate
ES-4	7	7	7
ST	1	1	1
Subtotal	8	8	8
GS/GM-15	25	25	25
GS/GM-14	48	48	48
GS/GM-13	36	36	36
GS-12	42	42	42
GS-11	31	31	31
GS-10	1	1	1
GS-9	30	30	30
GS-8	12	12	12
GS-7	46	46	46
GS-6	25	25	25
GS-5	24	24	24
GS-4	13	13	13
GS-3	3	3	3
Subtotal	336	336	336
Grades established by an act of July 1, 1944 (42 U.S.C., 270):			
SES Equivalent	1	1	1
Director grade	23	23	23
Senior grade	6	6	6
Full grade	4	4	4
Senior assistant grade	2	2	2
Subtotal	36	36	36
Ungraded	6	6	6
Total permanent positions	386	386	386

FRIDAY, MARCH 14, 1986.

NATIONAL EYE INSTITUTE

WITNESSES

DR. CARL KUPFER, M.D., DIRECTOR, NATIONAL EYE INSTITUTE

EDWARD McMANUS, DEPUTY DIRECTOR, NATIONAL EYE INSTITUTE

DR. JACK McLAUGHLIN, ACTING DEPUTY ASSOCIATE DIRECTOR FOR EXTRAMURAL AND COLLABORATIVE PROGRAMS, NATIONAL EYE INSTITUTE

KENNETH O. COOKE, EXECUTIVE OFFICER, NATIONAL EYE INSTITUTE

CARMEN M. RICHARDSON, BUDGET OFFICER, NATIONAL EYE INSTITUTE

DENNIS P. WILLIAMS, ACTING DEPUTY ASSISTANT SECRETARY, BUDGET, DHHS

Mr. NATCHER. Next we take up the budget for the National Eye Institute. We have before the committee Dr. Carl Kupfer, the Director. Dr. Kupfer, it is a pleasure to have you back before the committee. You appeared before us on one or two other occasions.

Dr. KUPFER. Yes, sir.

Mr. NATCHER. We are glad to have you. Before you proceed with your statement, tell us who you have at the table.

Dr. KUPFER. Mr. Edward McManus, Deputy Director; Dr Jack McLaughlin, Acting Deputy Associate Director; Mr. Kenneth Cooke, Executive Officer; and Ms. Carmen Richardson, Budget Officer.

COST EFFECTIVE RESEARCH PROGRAMS

Mr. NATCHER. Glad to have all of you before the committee at this time. Dr. Kupfer, we will be pleased to hear from you.

Dr. KUPFER. Thank you, sir.

I have submitted my opening statement for the record and would like to present just a short statement, if I may.

Eleven million people have to endure the effects of a permanent visual disability, but the burden is not theirs alone. Professional care and special services for people with eye problems cost our Nation an estimated $16 billion a year.

Research supported by the National Eye Institute can help to reduce these economic and social costs.

Today I would like to tell you about one of the National Eye Institute's most cost effective research programs, our retinal disease program. Diseases affecting the retina of the eye are among the most serious of all eye problems and one of the most common causes of retinal diseases is diabetes.

Over a period of years it can cause a series of harmful changes that culminate in profound visual loss. But even when the visual impairment is more subtle, the diabetic's quality of life can become drastically altered. As the individual's vision becomes blurred, he or she may no longer be able to read or drive an automobile.

Research supported by the National Eye Institute is aimed at overcoming the ocular problems which eventually affect up to 40 percent of our nation's ten to eleven million diabetics.

This past year the National Eye Institute had exciting news for diabetics. The first results to emerge from the early treatment of diabetic retinopathy study yielded information that could be of immediate benefit to many of those still in the early stages of diabetic eye disease.

The results show that it is possible to halt or even reverse the effects of diabetic macular edema, a condition which can cause blurring and serious visual loss. The investigators found that treatment with a laser cut in half their patients' risk of losing vision.

The condition being treated in this study and the laser technique employed are quite distinct from those involved in the Diabetic Retinopathy Study, the results of which I reported to this committee several years ago.

But taken together, the results of these two clinical trials provide a compelling reason for diabetics to have regular eye examinations to find out if they have a condition requiring some form of laser treatment to preserve their vision.

If the findings from these two studies are applied in this way and the patients treated appropriately, the net savings to society could total more than half a billion dollars a year.

Mr. Chairman, thank you for the opportunity to appear before your committee. I would be happy to answer any questions.

The request of the National Eye Institute for the 1987 fiscal year is $179,201,100.

[The statement of Dr. Kupfer follows:]

DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health
Statement of the Director
National Eye Institute

One of every twenty Americans is visually impaired. This means eleven million people--men and women, senior citizens and children, blacks and whites--have to endure the effects of a permanent visual disability. But the burden is not theirs alone. Professional care and special services for people with eye problems cost our nation an estimated $16 billion a year.

Among the most serious of these eye problems are diseases affecting the retina. If this delicate tissue lining the inside of the eye is damaged, visual impairment, and even blindness, may result. Diabetes is a common cause of retinal destruction, and over a period of years it can cause a series of harmful changes that culminate in profound visual loss. But even when the visual impairment is more subtle, the diabetic patient's quality of life can be drastically altered as vision becomes just blurred enough to prohibit reading or driving a car. The National Eye Institute (NEI) supports research aimed at overcoming the broad spectrum of diabetes-induced ocular problems which eventually affect up to 40 percent of our Nation's 10 to 11 million diabetics.

This past year, the NEI had exciting news for our diabetic citizens. The first results to emerge from the Early Treatment Diabetic Retinopathy Study (ETDRS) yielded information that could be of immediate benefit to many of those still in the early stages of diabetic eye disease. The results showed that focal treatment with a laser can halt or even reverse the relatively mild reduction in visual acuity caused by macular edema. The objective of focal laser treatment is to coagulate tissue that is leaking fluid, causing retinal swelling and blurring of vision. In this national collaborative study involving eye care centers in 15 states, half of the eyes with macular edema underwent laser therapy initially, and half did not. After three years, only 12 percent of eyes in the treated group had lost a significant amount of visual acuity, whereas 24 percent of those in the untreated group had done so. In other words, laser photocoagulation cut in half the risk of visual loss in these patients.

To benefit from laser therapy, however, people with diabetes must have regular eye examinations to find out if this potentially sight-saving treatment is needed. The public health implications of this are enormous. Undoubtedly, the number of diabetics who are eligible for, and seek, some type of laser treatment to preserve their eyesight will increase. On the other hand, we are now able to prevent visual loss and disability in more diabetics. The net savings to society from successful application of this technique for macular edema alone amounts to nearly $100 million a year.

This year, there was important news also for the few diabetics who may someday face one of the most devastating events in the progression of diabetic retinopathy--a severe vitreous hemorrhage. When this occurs, the vitreous gel filling the center of the eyeball becomes clouded with blood. Permanent visual loss or blindness may result. In the past, surgeons had to make a decision about surgery in these patients without knowing whether it was better to wait and see if the hemorrhage cleared up on its own, or to risk a delicate operation to remove the blood and scar tissue from the center of the eye.

These two approaches--immediate versus deferred surgery--to management of a vitreous hemorrhage which has caused serious loss of vision were compared in an NEI-supported clinical trial. The investigators found that 25 percent of eyes which underwent early surgery ended up with relatively good visual acuity, while only 15 percent of those in the deferred treatment group did so. For patients who had juvenile onset diabetes, the beneficial effect of early treatment was even more remarkable. In these eyes, three times as many in the early treatment group achieved good results (36 percent compared to 12 percent in the deferred treatment group). The conclusion: surgery performed soon after a serious hemorrhage can improve the chances for recovery of good vision in selected patients.

As you can see from these two clinical trials--and from our original Diabetic Retinopathy Study--we have accomplished a great deal in recent years when it comes to determining the most successful treatment strategies for a broad range of diabetic eye problems. In the future, we hope we will also be able to offer diabetics an effective means of preventing altogether the ocular complications of this disease. A major clinical trial is now underway to determine whether the drug sorbinil can slow or block the development of diabetes-associated eye and nerve damage. When this Sorbinil Retinopathy Trial was initiated, you may recall that I said one of the most gratifying aspects of the study is that it represents the culmination of years of basic research in the laboratories of the National Eye Institute. From pioneering work delineating the role an enzyme called aldose reductase plays in the development of diabetic complications, we have progressed to clinical evaluation of a drug that inhibits this enzyme and holds promise of interrupting the disease process. I am pleased to report that during the past year, patient recruitment was nearly completed. The enrollment goal of 600 patients will be reached soon, and the study will proceed towards its long-term scientific goal. If sorbinil proves effective, this drug and ones like it will revolutionize the management of diabetes and dramatically improve the outlook for people with this disease.

Even further in the future, there is a possibility of using treatments derived from recombinant DNA technology to protect diabetics from complications. In molecular genetic research going on right now in the NEI's laboratories, investigators are attempting to locate and isolate the actual genes which dictate the production of aldose reductase. Finding a way to interfere with the activity of these genes would give us an alternate method for blocking the onset of diabetes-associated tissue damage.

Molecular genetics is also being employed in the study of hereditary retinal disorders such as the retinitis pigmentosas. Scientists are trying to obtain more information about the underlying causes of this family of diseases in the expectation that this knowledge will make it possible to halt or prevent the process of retinal cell breakdown that leads to blindness. This year, NEI grantees took a significant step toward this goal. They confirmed and refined earlier estimates of the location of the gene that causes one specific type of retinitis pigmentosa. And now the genes responsible for other types are being sought. We hope that this research will clear the way to direct study of the defective genes, resulting in a much better understanding of the disease process and, eventually, gene therapy for the disorder.

We are also continuing to conduct and support basic research on the neurobiology of vision, a field which has proven to be one of the most scientifically fertile areas in the whole rapidly developing discipline of neurobiology. Within the last year, studies sponsored by the NEI have led to a better understanding of the function of retinal photoreceptors--the critically important nerve cells that give the visual system its capacity to detect light. For a long time we have known that these cells work by absorbing incoming light rays and then firing off electrical impulses in response. But the intermediate steps in this process, called transduction, have been unclear. There is a pressing need to further our understanding of visual transduction because malfunctions in this process can lead to irreversible visual loss. We anticipate that new knowledge in this area will bring us closer to comprehending the many sight-impairing diseases marked by abnormalities in the retina's responses to light. But in addition, research on transduction in retinal cells is expected to yield information about normal and abnormal neural signal transduction in all sensory systems of the body. Because the retina has proved to be such a good model in this regard, scientists in many other fields have recently turned their attention to the visual system, joining forces with vision scientists in trying to unravel the mysteries of transduction in retinal photoreceptors.

At the beginning of my presentation today, I described how two NEI-supported national collaborative studies had led to improved treatment of diabetic eye disease. Now I would like to tell you about a new clinical trial which may someday provide the basis for better management of retinopathy of prematurity, a disease that blinds many of the very smallest premature infants. The study will evaluate cryotherapy as a treatment for infants whose disease has progressed far enough that it threatens to destroy the retina. Although there is evidence to suggest cryosurgery might halt potentially blinding retinal changes, doctors caring for these babies need to know with certainty whether the technique is beneficial, what the risks are, and whether it is possible to tell in advance which babies will benefit from the procedure.

Before concluding my remarks today, I would like to mention the important role program planning plays in helping the National Eye Institute to decide whether to sponsor research like the two new clinical trials described above. Thanks to our ongoing program planning efforts, we are able to pinpoint where research is needed most, where the scientific opportunities are greatest, and where we would expect to receive the biggest return on our investment in terms of improving the prevention and treatment of blinding eye diseases. We are currently updating our 5-year plan, which covers the years 1983-1987, to take into account recent scientific advances and fresh opportunities in various areas of vision research. We will be sure to transmit a copy of this document to the Committee as soon as it is completed, probably in April. Through this planning process, we will maintain the careful but flexible investment strategy that has helped to make our program so productive thus far. In this way, I believe the National Eye Institute will be able to maintain the momentum of scientific achievements that have been such a striking feature of vision research over the past decade.

Mr. Chairman, the 1987 budget request for the National Eye Institute is $179,201,000.

I will be happy to answer any questions.

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Honors and Awards: Editorial Board, Investigative Ophthalmology, 1969-1977. Editorial Board, American Journal of Ophthalmology, 1971 to present. Member, Scientific Advisory Committee, Fight for Sight, Inc., 1971 to present. The Secretary's Special Citation, Department of Health, Education, and Welfare, April 1972. The Superior Service Award, Department of Health, Education,and Welfare, May 1974. Ticho Memorial Lecture, September 1974. Migel Medal, American Foundation for the Blind, October 28, 1976. Public Service Award in Ophthalmology, American Academy of Ophthalmology and Otolaryngology, October 1977. Speaker, Glenn A. Fry Award Lecture, American Academy of Optometry, December 1981. Senior Executive Service Bonus, Department of Health and Human Services, 1981. Johns Hopkins Society of Scholars, Johns Hopkins University, May 1982. Honorary Doctor of Science Degree, Scheie Eye Institute, University of Pennsylvania, November 1982. Member, Institute of Medicine, January 1983 to present. Speakér, XIV Jules Stein Lecture, Los Angeles, California, April 1983. Recipient, Special Award of Honor, The Juvenile Diabetes Foundation, June 1983. Recipient, David Rumbough Memorial Scientific Award, The Juvenile Diabetes Foundation, June 1983. Recipient, Presidential Rank Award of Meritorious Executives, 1983. Lecture, New York Academy of Medicine, New York, N.Y., March 1984. Bowman Lecture, The Ophthalmological Society of the United Kingdom, London, England, April 1984. Recipient, The Lighthouse Pisart Vision Award, October 1984. Lecture, Howard University Hospital, Washington, D.C., December 1984. Member, Board of Trustees, Helen Keller International Inc., 1975 to present. Coordinator for USA, US-Japan Collaborative Agreement in Vision Research, 1976-1982. Organizer, Oxford Assembly, International Agency for the Prevention of Blindness, (IAPB) 1978. Coordinator for USA, Priority Area "Eye Diseases," US-USSR Program for Health Cooperation, 1978-1981. Speaker, General Assembly of the World Council for the Welfare of the Blind, Antwerp, August 1979. Director, WHO Collaborating Center for the Prevention of Blindness, National Eye Institute, Bethesda, MD, 1979. President, IAPB, 1982 to present.

ALDOSE REDUCTASE INHIBITORS

Mr. NATCHER. Now, Doctor, thank you. Your statement tells us a major clinical trial is underway to determine whether the drug sorbinil can slow or block the development of diabetes-associated nerve and eye damage. A recent article in the Wall Street Journal tells us that scientists including Dr. Kinoshita have doubts about the effectiveness of the drug.

Are you having any second thoughts, Doctor, about whether to proceed with the sorbinil trial? Any second thoughts about it, Doctor?

Dr. KUPFER. I am glad you referred to this, sir, because it gives me an opportunity to give you a little background on the clinical trial and to comment on the article that did appear in the newspaper you referred to.

Let me start by saying that Dr. Kinoshita is the scientist who is responsible for developing the research base, if you will, on which this clinical trial was developed.

He is intimately involved with pursuing research on these drugs which inhibit a specific enzyme, aldose reductase, and he is very seriously committed to continuing this activity. In fact, to put it very bluntly I would say he was misquoted in this particular article.

Perhaps I could provide a little background information. We know that the enzyme aldose reductase is very much involved in the development of complications from diabetes. It is found in the lens, where it results in cataracts in diabetics; in the retina, where it contributes to retinopathy; in the nerves where it produces neuropathy; and even more exciting perhaps, in the kidney where it leads to nephropathy and is a major cause of death in diabetics. This theory about the role of aldose reductase has been developed over the past 25 years through research conducted by Dr. Kinoshita and his research team.

On the basis of research implicating this enzyme, Dr. Kinoshita worked in his own laboratory, as well as with a number of drug firms, to produce compounds that inhibit aldose reductase—and they have been successful. One of the first compounds to be developed was sorbinil by Pfizer, a drug firm. We began entering into negotiations with Pfizer about three years ago.

I personally felt motivated as a representative of the Federal Government to bring these two sectors—the public and private—together.

Pfizer is now providing 95 percent of the financial support for this clinical trial. We are providing some scientific surveillance.

The recruitment of some 600 patients has almost been concluded. The trial is looking at opportunities for preventing or slowing down the development of diabetic complications not only in the retina, but also in the nerves. I personally am very enthusiastic, and I have great hopes that this approach to preventing complications in diabetes may revolutionize the entire field of diabetes management and bring great hope to patients with this disease.

Several other drugs have been developed which inhibit aldose reductase and they too are beginning to be tested in clinical trials. So in a sense Dr. Kinoshita's work has opened up an entirely new area of research and holds great promise for the diabetes community.

OTHER APPROACHES TO CONTROLLING ALDOSE REDUCTASE

Mr. NATCHER. Now, Doctor, as you know, the Wall Street Journal article also says Dr. Kinoshita and a group of researchers in your institute have abandoned work on drugs of this type and are working, are searching for a gene instead.

Dr. Kinoshita is quoted as saying, and I quote, "We think by controlling the gene we can develop more effective and safer therapy. In the future we may look at the ARI drugs as a very primitive approach."

What about that now, Doctor?

Dr. KUPFER. Well, sir, I think that scientists who are amongst the most talented never put all their money on one horse. I think there are many approaches that are being pursued simultaneously including Dr. Kinoshita's current line of research.

Certainly the short term approach is to demonstrate that inhibition of this aldose reductase, in fact, can slow down or prevent the complications of diabetes.

At the same time, however, Dr. Kinoshita and his colleagues are using other approaches as well. We are looking at new inhibitors that are what we would call irreversible. In other words, instead of having to be taken every day or even every week, they might be taken every two or three weeks. In addition to these new inhibitors being developed, for the very long-term there is research going on using recombinant DNA technology to find ways of turning off the gene that produces the aldose reductase. But as I said this is a very long-term goal.

I think Dr. Kinoshita is to be commended for balancing short term objectives with long term goals and bringing both to bear on this very important problem.

NATURE OF COLLABORATION WITH DRUG FIRMS

Mr. NATCHER. Dr. Kupfer, how do you deal with a situation in which scientific questions are caused by a certain line of research, especially when a drug company is involved?

How difficult is it to switch resources to something else? What do you do, Doctor?

Dr. KUPFER. We have had very good interactions with a number of drug companies. The basis—and strength—of our relationship has been that each brings to the table certain resources. The drug companies bring the financial resources; they bring the need to develop certain drugs that are important from a public health and commercial point of view; and they bring other resources such as groups of investigators.

On the other hand, the National Eye Institute has the scientific expertise and is also interested in furthering advances in a particular field because of the public health implications of a particular disease. When there are advantages for both sides to collaborate, we then sit down, draw up a collaborative agreement which spells out very clearly what the relationship of the two organizations will be, and then proceed.

We have done this in the case of the sorbinil study where Pfizer has provided the resources and the NEI provides the scientific surveillance. We are also doing it in terms of individual scientists whose work at the National Eye Institute is sponsored by the drug firms. While at the NEI, they are pursuing research that is going to broaden our capability of attacking many very important problems in eye disease such as cataract and diabetes.

NIH RESEARCH PROJECT GRANT LEVELS

Mr. **NATCHER**. Dr. Kupfer, you have been at NIH for some time. You are familiar with last year's controversy over the number of research grants to be funded out of the 1985 appropriation. You know that in response to the proposal to stretch a portion of the 1985 appropriation over two years thereby reducing the number of grants to be funded, the committee was forced to specify the number of competing grants, 6200, in appropriation language.

In the 1986 Act we felt we had to do this again. Now, we have before us a proposal to eliminate the legislative requirement to fund no fewer than 6100 competing grants in 1986. We also have before us a proposal to include in the 1987 bill a requirement that no fewer than 19,400 competing and non-competing awards be funded by NIH and the Alcohol, Drug Abuse, Mental Health Administration in 1987. Dr. Kupfer, if you will please give us your frank appraisal of these two proposals with respect to number of grants.

Dr. **KUPFER**. Perhaps I could address it in two separate ways. I think specifying a number does serve a purpose. It does focus attention on the magnitude of the research effort that is required. And, therefore, I think numbers do help us to focus on what is needed.

But I think superimposed on those numbers should be the ability to pursue new research opportunities that come at times when we can't anticipate them. If one can superimpose on the numbers additional flexibility to take advantage of new opportunities as they arise, then I think this would be an appropriate way of approaching this problem.

Mr. **NATCHER**. What do you think will be the reaction of the scientific community to these proposals? How do they feel about it?

We talk to them from time to time, Doctor. In fact, I have talked to some in the last ten days. Just generally speaking, how would they feel about it?

Dr. **KUPFER**. Recently I attended a meeting of university professors in ophthalmology and I think they would share this general feeling, that there is a value in specifying numbers as well as having the flexibility to respond to new research opportunities.

INDIRECT COSTS

Mr. **NATCHER**. Thank you. Now, on indirect costs, is there a general feeling among the scientists with whom you deal that indirect costs are eating up too large a share of the research dollar?

Dr. **KUPFER**. I think I would say that that perception is correct, sir.

Mr. NATCHER. Are you familiar with the Administration's proposal to cap overhead costs at 26 percent on April 1, 1986, and 20 percent on April 1, 1987?

Dr. KUPFER. Yes, sir.

Mr. NATCHER. Do you think the research scientists with whom you deal would generally support such a proposal?

Dr. KUPFER. Perhaps, sir, I might defer to Dr. Raub to answer for the entire research community.

Mr. NATCHER. What about it, Dr. Raub? What would be the feeling here?

You know, we need all the help we can get, Doctor. We have to mark this bill up.

We just want to find out generally. Go ahead.

Dr. RAUB. Sir, I believe you will get mixed reactions from the scientific community. Individual scientists are likely to favor almost any policy in the direction of reducing the payments for indirect costs if the result is to be able to make more grants.

On the other hand, many of those individual scientists are not at all familiar with the details of the cost that their universities and other employer organizations incur and, therefore, may be unsympathetic because they are not fully informed. Institutional administrators, on the other hand, with equal conviction, I am sure, will address the Administration as well as the Congress in raising concerns about both the specific levels of that proposed cap and the timing of it.

Mr. NATCHER. All right. Dr. Kupfer, did your Advisory Council make a similar proposal a few years ago in regard to placing a limit on indirect cost? Was this made several years ago?

Dr. KUPFER. Yes, sir. As a matter of fact, it was. One member of our National Advisory Committee wanted to raise this question for discussion. I believe that that really started the entire discussion, which I think has been a very healthy one, first involving our council, but very rapidly involving the National Institutes of Health. I believe an article was written for Science Magazine, and that too brought the discussion to the forefront.

Mr. NATCHER. Mr. Hoyer, I yield to you.

EFFECT OF SEQUESTRATION

Mr. HOYER. Thank you very much, Mr. Chairman.

Doctor, what effect will the sequestration have on the priorities in your Institute?

Dr. KUPFER. I think that sequestration will have a small, overall effect. Its main impact will be negotiating grants somewhat, so that the funded amounts may be somewhat less than they ordinarily would be—although as a general rule we do negotiate grants a little.

Mr. HOYER. Doctor, would it be accurate to conclude that the renegotiation of the grants will be generally at the level of a four to five percent decrease in what they otherwise would have been, the same kind of across-the-board cut as the 4.3 percent effect?

Dr. KUPFER. It would perhaps be a bit more with the sequestration because the first round of grants was awarded before the sequestration levels were determined. There was no further negotiation of that group and we will have to make it up in subsequent rounds.

FTES

Mr. HOYER. That is the same problem we had last year with the numbers of grants that were awarded. Now last year, Doctor, in answer to a question that I posed with reference to FTEs, you indicated there may be a problem. What is your FTE level at this point in time?

Dr. KUPFER. We have 203 FTEs at the present time, Mr. Hoyer.

Mr. HOYER. What does the 1987 budget provide for?

Dr. KUPFER. The same number, sir.

Mr. HOYER. You would expect, therefore, to be able to maintain the same complement that you now have?

Dr. KUPFER. Yes, sir.

Mr. HOYER. Doctor, what was your request to NIH?

Dr. KUPFER. For the fiscal year 1987 it was $225 million. There was a request also for 245 FTEs.

Mr. HOYER. Doctor, last year's request caused a retrenchment in your complement. I don't have the specific figures in front of me, but in 1985 did you have a greater complement? Can you give me 1984 and 1985 so I can get a view of the flow?

Dr. KUPFER. Yes, sir. In 1984, I believe it was 234 FTEs and in 1985 it was 215.

Mr. HOYER. So you are down to 203 now or little over a ten percent cut. But you do not expect any cut in 1987.

Dr. KUPFER. There is none proposed in our budget, sir.

Mr. NATCHER. You didn't answer my question which leads me to believe as a trial attorney that——

Dr. KUPFER. No. I don't think there is any reason to think that it will go below 203. That is the figure that is in the budget request for 1987.

Mr. HOYER. I understand. You don't expect to have additional cuts. You don't expect to have OMB come back and say to you that you are going to have less employees. Really, we need to save a little more money and tighten our belts, so freeze your hiring levels and don't fill vacated positions?

Dr. KUPFER. We haven't seen any indication that that would be the case.

Mr. HOYER. Fine. You don't expect it then and that is good. Is 203 a complement that is sufficient to accomplish effectively the objectives of your institute?

Dr. KUPFER. Yes, sir. Given the reduction, we have taken further steps to provide the necessary support and I think we can live with the 203, yes, sir.

RADIAL KERATOTOMY

Mr. HOYER. Now, Doctor, last year and you have spoken about it here, on surgery for nearsightedness, are there any new developments this year?

Dr. KUPFER. I believe last year I was able to report the one year results from the clinical trial that was being conducted on the radial keratotomy study, the so called Prospective Evaluation of

Radial Keratotomy or PERK. At that time, if you recall, the one year results indicated that about three-quarters of the patients had had an improvement in the amount of nearsightedness and these results compared very well with other studies that had been done.

More recently, we have some two-year data. Now only about two-thirds of the patients have been stabilized. And one-third are either continuing to develop less and less nearsightedness and are becoming farsighted, or in some cases their nearsightedness has returned.

In other words, one-third of the patients are fluctuating and have not stabilized. We are concerned with whether this technique really is as predictable as we had hoped it would be. And the fact it does lack this predictability encourages us more to follow these patients for a longer time.

Mr. HOYER. Obviously, predictability is a question and stability of the result. Is the procedure itself safe?

Dr. KUPFER. Like so many surgical procedures, whenever one embarks on a surgical intervention, there is always an element of risk. As procedures go, in the hands of a competent ophthalmic surgeon, I think it has very little risk.

But I hasten to add—we must keep in mind that we are operating on a perfectly healthy, normal cornea, and this surgical intervention does have non-surgical alternatives such as contact lenses and spectacle lenses.

This is not the case with cataract. So one must look at the risk, as small as it is, in a different context than one looks at the risk of a cataract extraction. After all, the consequences of not undergoing cataract surgery is not being able to see with that eye.

With radial keratotomy we really must be concerned with the long-term side effects and, therefore, this project is continuing for a number of years.

PRESBYOPIA

Mr. HOYER. Doctor, what is the prospect of research resulting in the stopping of the deterioration of the use of the muscles of the eye which is, I guess, the most common eye problem? Describe for me—the reason I have to use these glasses. Is my muscle lazy; is that correct?

Dr. KUPFER. Yes, sir.

Mr. HOYER. It won't in effect focus in well enough in the close reading operation which I guess is a pretty lay person's definition of why I need these glasses. What is the prospect of us ever overcoming that?

Do you have any thoughts that that will occur? Something to reverse that or strengthen the muscle or something?

Dr. KUPFER. Are you referring, sir, to the need for reading glasses as one gets into their forties and fifties?

Mr. HOYER. Yes, sir.

Dr. KUPFER. This can be viewed as a reduction in the flexibility of the lens. In the young person the lens has the ability to change its shape. As one holds something closer it becomes more spherical.

That ability is reduced somewhere in the forties and fifties. I think as we come to understand more about what changes occur with age at the molecular biological level, it may be possible to slow down this process clinically. But again, this depends on our learning more about the basic aging process in the eye.

Now, there are obviously other ways of approaching this problem and of course the easiest is the use of reading glasses.

New procedures are being considered and devised to try to replace reading glasses with more permanent types of surgical interventions but I think they are very experimental. I would not want to go into them at the moment.

Mr. HOYER. Thank you very much, Doctor.

Thank you, Mr. Chairman.

MYOPIA

Mr. NATCHER. Yes, sir.

Now, Doctor, is it true that the incidence of nearsightedness is increasing every year and that eventually everyone may have to wear glasses? What do you think, Doctor?

Dr. KUPFER. I don't think nearsightedness is increasing. Eventually, I think we *all* need to wear glasses to help us read close up as we pass the age of 40 or 50. Even those who have been very nearsighted will eventually have to have some help of this sort.

So, following up on the comment of Mr. Hoyer, there are changes in the eye that require the help of glasses as we get into the forties and fifties and sixties. As far as nearsightedness itself is concerned, I am not aware of any data to suggest its incidence is increasing.

Mr. NATCHER. Any additional questions?

Mr. HOYER. No further questions, Mr. Chairman.

Thank you very much.

Mr. NATCHER. Dr. Kupfer, we want to thank you for your appearance before our committee at this time along with your associates. This has been a good hearing and we appreciate it.

We will recess now until ten o'clock Tuesday morning.

[The following questions were submitted to be answered for the record:]

GROWTH AND DEVELOPMENT OF NEI PROGRAMS

Mr. Conte. Dr. Kupfer, how long have you been at the Eye Institute and how long have you been director now?

Dr. Kupfer. I have been the Director of the National Eye Institute for almost sixteen years.

Mr. Conte. What kind of changes have you seen at the Institute and the kinds of research going on at the Institute over that time frame, Doctor?

Dr. Kupfer. The greatest change, the one I find the most gratifying, is simply the tremendous growth in funding for vision research over the past decade and a half. I have no doubt that such growth would never have occurred without Congress' creation of a separate National Eye Institute and the subsequent unwavering support of the Congress for our programs ever since. One measure of such growth is the increase in the number of research project grants, the R01's, which has grown from 353 in FY 1970 to 1,068 in FY 1985. Early on, we determined that this mechanism, which more than any other encourages the initiative and creativity of the individual scientist while providing us the maximum flexibility in terms of allocating research dollars, would have to be the mainstay of our support. Therefore, we set out early to reduce our reliance on other mechanisms such as contracts and umbrella grants, using them only in those relatively few circumstances where they were warranted.

Another change has been the development of a strong intramural program of vision research at NIH. The advantages of such a program are many, but I think that its most important function is to provide leadership to the national eye research community in important emerging areas of research. Not only can the intramural program serve as a demonstration site and proving ground for such activities as the application of new techniques in immunology, molecular biology, and neuroscience, it plays an invaluable role in training outside investigators in these areas who then return to their own institutions and establish their own programs.

A major change, which has had an enormous impact on the health and well-being of the American people, has been the institution of a series of clinical trials of new diagnostic and therapeutic methods for major causes of blindness. When the NEI was created there had been only one such trial in the entire history of eye research. Today, there are 28 trials ongoing, involving 62 departments of ophthalmology, hundreds of referring practitioners, and thousands of patients. The NEI staff has played and continues to play a major role in the development and monitoring of many of these trials, but what is particularly gratifying to me has been the development of expertise in and support for clinical trials within the vision research community, and indeed among the eye care community as a whole. These trials have demonstrated that the scientific method can be applied to answering important clinical questions, even to the evaluation of new surgical techniques, thereby hastening the translation of scientific knowledge into medical practice. Several trials have already yielded knowledge which daily is saving many people from blindness.

A fourth change has been the emergence of vision research as a vital scientific discipline in its own right which not only incorporates and applies to the visual system advances in other fields of bioscience, but actually is at the cutting edge in several areas of inquiry, most notably in the neurosciences and in diabetes research. Some of the brightest minds in all of science are working today in the visual system, and the NEI is supporting their work. Work done in the eye and visual pathways to the brain frequently has important implications for problems involving other organ systems or the body as a whole. Today, more than ever, the eye is truly the window of the body for what it is telling us about the nature of our biological selves.

EMPHASIS ON RESEARCH PROJECT GRANTS

Mr. Conte. The Institute, as I have understood it, puts a lot of emphasis on research grants, compared to other mechanisms, and that is one of the reasons that it has a relatively high award rate. What percentage of your appropriation goes into research grants?

Dr. Kupfer. The National Eye Institute allocates approximately 77 percent of the total budget for investigator-initiated research project grants.

Mr. Conte. Doctor, and how does that compare with the other institutes at NIH?

Dr. Kupfer. The NIH obligates approximately 58 percent of the total budget for these grants.

Mr. Conte. Why do you think that is the most appropriate use of resources Doctor?

Dr. Kupfer. Because investigator-initiated research project grants are assessed individually for scientific merit and relevance every three to five years, they can be continued or terminated depending on their relative quality and importance to the overall research effort. This kind of flexibility is appropriate because it enables us to sustain a vision research program which can be restructured easily to pursue promising new ideas.

Mr. Conte. So, in any attempt to limit the number of new and competing grants, the Eye Institute suffers disproportionately, is that correct?

Dr. Kupfer. Yes, that is correct. Overall funding policies that focus on research project grants affect a very large part of our total program.

Mr. Conte. How many grants did you fund in FY 1985--new and competing grants, that is?

Dr. Kupfer. In 1985 the NEI funded 367 new and competing renewal research project grants.

Mr. Conte. Under the FY 1986 Appropriation, how many grants would you fund, and how does that compare with the revised FY 1986 budget proposal?

Dr. Kupfer. Under the FY 1986 Appropriation 358 competing projects would be supported as compared to 331 in the 1986 revised budget.

Mr. Conte. Last year, for FY 1986, the administration proposed 249 new and competing grants, and as we just went over, Congress approved a good number more. This year, for FY 1987, the budget proposal goes right back to 250, is that correct?

Dr. Kupfer. Yes, in 1986 the budget request included 249 new and competing grants and Congress appropriated 358. The 1987 budget request provides funds for 250 new and competing renewal awards.

Mr. Conte. And so the net result would be to take the number of new and competing grants from 367 in FY 1985 down to 250 in FY 1987, a reduction of nearly a third, is that correct?

Dr. Kupfer. Yes, your statement is correct, the Institute would fund 117 fewer competing grants in 1987 than were paid in 1985.

Mr. Conte. I would conclude that this would substantially restrict the ability of the Institute to move vision research forward. Would you have any reason to dispute that conclusion?

Dr. Kupfer. There will be some delays but many important proposals will be continued in 1987.

CATARACT SURGERY

Mr. Conte. We hear a lot about the improvements that have been made in the removal of cataracts, which has now become an outpatient procedure, and makes a dramatic difference for a lot of elderly folks. Yet, we hear of problems in surgeons overcharging or taking kickbacks, and sometimes complaints from elderly folks about not being taken care of in the hospital. Have you run across any problems through the Institute's work in this area, in the way this new development has been put into practice?

Dr. Kupfer. These conflicts concerning the delivery of cataract care are within the purview of other components of the Federal Government, particularly the Health Care Financing Administration. But they also concern the National Eye Institute. In fact, they have reinforced an opinion that we have held for years. That opinion is that surgery--however sophisticated, successful and accessible it may be--should not be considered the ideal way of approaching the problem of cataract. In the long run it would be much better to find a means of preventing the development of cataracts, or at least slowing their progression, so that an individual will have less risk of experiencing the sort of lens changes that make surgery necessary. The NEI is very actively fostering research on cataract and its underlying mechanisms in the hope of making prevention and non-surgical treatment a reality in the not-too-distant future.

EYE PROPHYLAXIS IN THE NEWBORN

Mr. Conte. The stories that really break your heart, though, are the stories of problems in newborn infants. Last year we talked about the fact that some 75,000 infants are born with the sexually transmitted disease chlamydia infecting their eyes. Last year, you told us that some pretty impressive gains were being made, particularly in diagnosing it, and you also stated that you felt you had good resources to address it. What can you tell us about this, this year, Dr. Kupfer?

Dr. Kupfer. The National Eye Institute has recently initiated a single-center, controlled clinical trial in Seattle to evaluate the effectiveness of prophylactic treatments currently used in newborns to prevent conjunctivitis. Infants entering the study will be randomly assigned to treatment with silver nitrate solution, treatment with erythromycin ointment, or no ocular prophylaxis at birth. The ocular health of all infants in the study will be evaluated. Because the majority of cases of conjunctivitis seen in newborns in that city are the result of chlamydial infections of the mothers, the results of this study will have a profound influence on the future treatment of this eye disease in the United States.

RETINOPATHY OF PREMATURITY

Mr. Conte. And the other one that you read about is blindness of infants born prematurely. An article in the Post last January presented the problem as an epidemic of unknown proportions, but put forth some figures that of 20,000 infants born at less than 3.3 pounds, 2,000 would be partly blind, and more than 500 would become legally blind. In your statement you mentioned something about a new technology called "cryosurgery." Could you translate that one for us, Doctor, and tell us what you think this new technique might be able to accomplish?

Dr. Kupfer. Cryosurgery is the use of a very cold surgical probe to freeze tissue. The retina--the light-sensitive layer of tissue inside the back of the eye, with which we see--is highly vascularized. The vascularization of the retina occurs during gestation and under normal conditions is just about complete at nine months, at birth. The premature infant has an incompletely vascularized retina. In the infant with a severe case of retinal disease called retinopathy of prematurity, there is a ridge of tissue and blood vessels at the periphery of the retina which can bleed into the eye and cause total retinal detachment. We are now conducting a clinical trial at 24 centers across the US to find out whether freezing this ridge--from the outside of the eyeball--in the highest risk infants, is of benefit.

LOW VISION

Mr. Conte. Over the past couple of years, we've talked about the need to address the needs of people with low vision, not only in terms of medical techniques to improve vision, but in terms of ways to improve their ability to function, and the need to promote more research and researchers in this area. Have you had much success in stimulating research in this area?

Dr. Kupfer. During the past year the NEI issued a special Request for Applications on research to provide a profile of visual function in low vision patients. This special program elicited 20 applications and will probably result in 6 new awards during 1986. Topic areas addressed by projects in this area include the development of reading aids, visual requirements for mobility, control of eye movements in retinal degeneration, and the ability to recognize human faces.

Applications of electronic technologies are leading to devices that will improve the quality of life of visually impaired persons. In particular, personal computer technology is being applied to the development of reading aids that magnify or present in modified format ordinary reading materials. This is sometimes combined with synthesized speech that can substitute for cumbersome braille output. Optical character recognition technology is also being used to convert printed information to tactile or verbal output. There are also mobility aids under development that relay information on features of the environment, thus making it easier for a visually impaired person to move about.

Mr. Conte. We've also talked in the past about the fact that to find the researchers in this area and encourage them, you might have to go outside of the usual biomedical researchers, and seek out professionals like bio-engineers. Have you been able to do that at all?

Dr. Kupfer. Yes, we have been successful in communicating to the field as a whole the necessity to incorporate multidisiplinary teams in the design and conduct of low vision research. Both in the applications received in responce to our RFA and in applications that have come in through the Small Business Innovative Research Program, inclusion of bioengineering as well as rehabilitation and computer or electronics expertise has become the norm.

EYE COMPLICATIONS OF DIABETES

Mr. Conte. In your statement, you talk a great deal about developments that will assist in the treatment and even now in the prevention of the complications of diabetes that affect vision. How many people have diabetes, and how many of those are likely to develop related eye dysfunctions?

Dr. Kupfer. Yes. The successes we have enjoyed in the treatment of diabetic retinopathy, and the prevention of its ocular sequelae, have depended heavily on advances in laser technology. Over the past few decades, ophthalmic researchers have worked closely with physicists and engineers in the refining and improving of laser technologies that can be be applied to treatment of the inside of the eye, even at the microsurgical level. As a further example, ophthalmologists and bio-engineers have been working together on the development of new techniques for diagnosing and assessing the conditions of intraocular tissues using very low levels of light. This new technology is essential to our better appreciation of some of the untoward events that occur in diabetic retinopathy, glaucoma, or aging-related macular degeneration.

We have also been actively collaborating with experts in other disciplines, such as pharmacology. For example, there is the project on aldose reductase inhibitors in diabetes, which we are participating in with Pfizer Inc.

Mr. Conte. How many do you think you'll be able to help with these developments?

Dr. Kupfer. There are approximately 10 million diabetics in this country. About 40% show at least mild signs of diabetic retinopathy, and about 3% have suffered severe visual loss because of it. Generally speaking, the longer a person has had diabetes, the greater the chances of developing diabetic retinopathy and visual loss.

The findings of the diabetic retinopathy study indicate that laser photocoagulation treatment of advanced proliferative diabetic retinopathy is today reducing by more than half the number of people who would have otherwise gone blind from this form of the disease. The findings this year from the Early Treatment Diabetic Retinopathy Study indicate that many patients with an early manifestation of diabetic retinopathy (macular edema) can be spared reductions in visual acuity with prompt laser treatment.

Mr. Conte. A lot of these developments related to diabetes are in the clinical trial phase, according to your statement. How important are clinical trials to what is going on in your institute, Doctor?

Dr. Kupfer. As I have already noted, the National Eye Institute has had some major successes in the past few years with respect to treatment of diseases like diabetic retinopathy, aging-related macular degeneration, branch vein occlusion, etc. These successes are the results of major nationwide clinical trials that we have supervised and supported. Our clinical trials program has served as a most effective vehicle for moving from the research of individual basic and clinical investigators to the development and testing of treatments using rigorous scientific methodologies which allow for the assessment of safety and efficacy in larger numbers of patients. We are particularly proud of our scientific and medical accomplishments in the area of clinical trials research.

CLINICAL TRIALS

Mr. Conte. Are there any ongoing clinical trials that will be impaired by the Gramm-Rudman-Hollings cutback or the budget proposal in FY 1987?

Dr. Kupfer. Funding for most of our ongoing clinical trials will be reduced by the Gramm-Rudman-Hollings cutback and the 1987 budget request. However, resources will be maintained at levels that ensure that the scientific integrity of the research will not be sacrificed.

Mr. Conte. Are there any approved clinical trials that you will not be able to start in FY 1986 or FY 1987 due to budgetary constraints?

Dr. Kupfer. We anticipate that the following and possibly other new clinical trials will be ready for funding in 1987.

	(In Thousands) 1987 Cost	Total Projected Cost
Central Retinal Vein Occlusion Study	$1,000	$5,000
Treatment of Optic Neuropathy with Steroids	1,500	8,000
Surgical Reattachment of the Retina in Advanced Severe Retinopathy of Prematurity	3,000	12,000
Evaluations of Epikeratophakia and Keratoprostheses as Treatments for Corneal Disorders	1,500	7,000
Surgical vs. Laser Management of Advanced Glaucoma	1,000	5,000
Total	8,000	37,000

Mr. Conte. One clinical trial I believe you have going on is as to whether the operation to correct nearsightedness is beneficial. Any results on this yet?

RADIAL KERATOTOMY

Dr. Kupfer. I am pleased to share the most recent findings from the Prospective Evaluation of Radial Keratotomy study which the NEI supports. Last September, the study released findings on the effects of radial keratotomy in hundreds of its patients who had undergone the operation two years earlier. These two-year data confirm earlier reports that radial keratotomy often is effective in correcting nearsightedness. But they also strengthen earlier findings that the outcome of the procedure is variable and cannot be predicted with certainty for an individual patient. For example, in a third of the patients in this study the degree of nearsightedness continued to change for more than a year after surgery. It was not possible to predict which patients would show such changes.

In addition, the results indicate that when radial keratotomy is performed in both eyes of an individual patient, the two eyes may show different outcomes, with one being more strongly corrected than the other. Such a disparity was noted in a fourth of the patients in this study. Also, the study found that when a radial keratotomy did not produce sufficient improvement in vision, a repeat procedure might give unexpected results: Four of the 42 eyes that had reoperations actually became more nearsighted as a result of the second surgery. Finally, in three eyes corneal infections related to radial keratotomy developed more than a year after the surgery.

In view of these two-year findings, the study's investigators are convinced that further evidence will be needed before the safety and efficacy of radial keratotomy can be assessed. The NEI concurs in that belief, and will continue to support research on this procedure.

PRESBYOPIA

Mr. Conte. Have you got anything to help us mature guys out, who have to wear these reading glasses to get their point across?

Dr. Kupfer. Eventually, as we reach the age of 40 or 50, I think we all need to wear glasses to help us read close up. Because of changes in the eye even those who have been nearsighted will need some help of this sort. As we learn more about the basic aging process in the eye, at the molecular biological levels, it may be possible to slow down this process clinically. At the present time the easiest way to treat this problem is to use reading glasses.

EXTENDED WEAR LENSES

Mr. Conte. And for the young, upwardly mobile, urban professionals in the crowd: What are the latest results on extended wear contact lenses? Stay away from them?

Dr. Kupfer. First, it should be noted that although the general view of extended wear contact lenses as being used by young adults has substantial validity, there now is increasing utilization of these lenses by older individuals. Within the last year there have been a number of reports of bacterial, viral and fungal infections associated with the use of extended wear lenses in people of various ages. However, the majority of individuals using extended wear lenses have not had these disorders. In many of the instances in which eye problems were found, it appeared that the patient was not following prescribed procedures for wearing such lenses or for cleaning and sterilizing them.

Mr. Conte. Are there any improvements we should be aware of with respect to contact lenses?

Dr. Kupfer. The newer developments in contact lens design have been primarily directed at older individuals. Bifocal lenses for people who need help with reading vision and toric lenses to correct astigmatism have received greater attention. Also, there has been increased production of soft contact lenses for people who have undergone cataract surgery.

EFFECT OF GRAMM-RUDMAN

Mr. Stokes. Dr. Kupfer, what areas of research will be affected by the 1986 Gramm-Rudman reductions of $8.389 million for your institute? Do you anticipate requesting any reprogramming in order to protect any high priority research activities from Gramm-Rudman reductions?

Dr. Kupfer. We are still reviewing our programs to identify potential problems so that we can submit a reprogramming if it is needed.

DIABETES RESEARCH

Mr. Stokes. Dr. Kupfer, given the great likelihood that a large number of individuals who develop diabetes will also be at risk of developing eye disorders, do you believe that the NIH, overall, is putting an adequate emphasis on diabetes research?

Dr. Kupfer. Overall, since the National Diabetes Mellitus Research and Education Act of 1974, the NIH has given considerable attention to diabetes. The recent creation of the National Institute of Diabetes, and Digestive and Kidney Diseases is further evidence of the NIH commitment to this devastating disease. As you are likely aware, the NEI has had a major commitment to diabetes-related research as well, with an annual program of clinical and basic research relative to the eye complications of diabetes in excess of $20 million for the past few years.

Mr. Stokes. What about your institute? What proportion of your budget is devoted to diabetes related research?

Dr. Kupfer. Approximately 12 percent of the total NEI budget is obligated for diabetes related research.

Mr. Stokes. What new advances can you report to us this year regarding diabetic retinopathy?

Dr. Kupfer. The National Eye Institute supports research aimed at overcoming a broad spectrum of diabetes-induced ocular problems which are believed to afflict as many as 40 percent of our nation's 10 to 11 million diabetics. This year, the NEI had exciting news for diabetics at both ends of the spectrum.

In early December, the first results to emerge from the Early Treatment Diabetic Retinopathy (ETDRS) were reported at a nationally televised news conference. The results showed that treatment with a laser could halt or even reverse the effects of macular edema in people who are still in the early stages of diabetic eye disease. Although the reduction in visual acuity may be relatively mild at this stage, the patient's quality of life can be dramatically affected if vision becomes too blurred for reading or driving a car. In this multicenter clinical trial, half of the patients underwent laser therapy initially and half did not. After three years, only 12 percent of eyes in the treated group had lost a significant amount of visual acuity, whereas 24 percent of those in the untreated group had done so. In other words, laser photocoagulation cut in half the risk of visual loss in these patients.

To benefit from laser therapy, however, people with diabetes must have regular eye examinations to find out if this potentially sight-saving treatment is needed. The public health implications of this are enormous. Undoubtedly, the number of diabetics who are eligible for, and seek, some type of laser treatment to preserve their eyesight will increase. On the other hand, we are now able to prevent visual loss and disability in more diabetics. The net savings to society from successful application of this technique for macular edema alone amounts to $100 million a year.

This year, there was good news also for diabetics at the opposite end of the spectrum, those who have experienced one of the most devastating events in the progression of diabetic retinopathy--a severe vitreous hemorrhage. When the vitreous gel filling the center of the eyeball becomes clouded with blood, permanent visual loss, even blindness, may result. In such a case, surgeons have not known whether it is better to wait a year to see if the hemorrhage clears up on its own, or to risk a delicate operation to remove the blood and scar tissue from the center of the eye.

These two approaches--immediate versus deferred surgery--to management of a vitreous hemorrhage which has caused serious loss of vision were compared in an NEI-supported clinical trial. The investigators found that 24.5 percent of eyes which underwent early surgery ended up with relatively good visual acuity, while only 15.2 percent of those in the deferred treatment group achieved such good results. For patients who had juvenile onset diabetes, the beneficial effect of early treatment was even more remarkable. In these eyes, 36 percent of the early treatment group, compared to 12 percent in the deferred treatment group, achieved good results. The news for diabetics then, is that surgery performed soon after a serious hemorrhage can improve the chances of a long term recovery of good vision.

AIDS RESEARCH

Mr. Stokes: I understand that the AIDS virus has been found in the tears of some AIDS victims, but not all AIDS patients. Could you comment on the significance of this finding? What other research are you conducting on AIDS?

Dr. Kupfer: Previous studies of AIDS patients had already demonstrated that the virus can be isolated from many tissues and body fluids, including blood and saliva. Thus the isolation of the virus from the tears of some AIDS patients is not unexpected. The Centers for Disease Control has published guidelines for use by eye care specialists and other eye health personnel who may be working with patients infected with the AIDS virus. These guidelines are designed to guard against any risk of transmission of the virus through routine ophthalmic procedures.

NEI scientists are continuing to study ocular manifestations of AIDS. This research is being conducted in collaboration with scientists from the National Institute of Allergy and Infectious Diseases, the National Cancer Institute, and the NIH Clinical Center. In these cooperative studies, the investigators are attempting to learn more about 1) the relationship between certain ocular manifestations of AIDS and the severity or rate of progression of the disease, 2) the extent to which ocular signs can be of value in monitoring the effects of experimental treatments, 3) the treatment of potentially blinding cytomegalovirus infections of the retina in AIDS patients, and 4) the distribution of the AIDS virus within the ocular tissues and fluids of the patients.

GLAUCOMA RESEARCH

Mr. Stokes. Dr. Kupfer, in past years, we have talked about the high incidence of glaucoma in blacks. Your budget justification states that glaucoma may be the major cause of blindness among black Americans. Can you update me on the 5-year study underway to study the disparity in the incidence of glaucoma between blacks and whites and the associated risk factors?

Dr. Kupfer. The epidemiologic study, "Racial Variations in Chronic Open-Angle Glaucoma", is just entering its third year. It is designed to determine the prevalence of this most common form of glaucoma in closely matched populations of blacks and whites in Baltimore. For years ophthalmologists have been under the impression that open-angle glaucoma is more prevalent and runs a more severe course in blacks than in whites. We anticipate that this new study will give us precise data bearing on this very important question. Approximately 80 percent of the black population targeted for interviews and eye examinations has been contacted and examined, and the survey will now swing to the comparable white group. Racial age and sex correlations and risk factor evaluation await completion of data acquisition. Further information on risk factors for glaucoma will be forthcoming from three other small studies, and from research investigating why some people with high intraocular pressures eventually develop the optic nerve and visual changes characteristic of glaucoma, while other people do not.

Mr. Stokes. Can you highlight any other studies that are underway with regard to glaucoma?

Dr. Kupfer. The National Eye Institute is supporting two multi-center clinical trials evaluating therapy of open-angle glaucoma. In the first, the benefits and risks of treating newly diagnosed glaucoma by immediate use of an argon laser are being compared with conventional treatment by use of eyedrops. This study, now in its third year, should reveal if the simpler, non-invasive laser treatment will eliminate or reduce the lifetime need for daily use of drugs and lessen the possibility that surgery will be required later. Because a recent study has shown that a majority of glaucoma patients fail to take their drugs as prescribed, there is more reason than ever to expect that a reduction in the need for drugs will significantly improve glaucoma therapy. Also, the ultimate costs of therapy should be greatly reduced.

In the second study, a drug treatment that may improve the outcome of glaucoma surgery in very high-risk cases is under investigation. In glaucoma, fluid fails to leave the eye as rapidly as it is formed, causing intraocular pressure to rise with resultant damage to the optic nerve and loss of vision. In the surgical procedure most commonly used to help these patients, the surgeon makes a tiny hole in the area of the eye through which intraocular fluid normally leaves; failure of the surgery is caused by formation of scar tissue which seals over this opening. Animal studies and preliminary findings in very high-risk human eyes have indicated that treatment of the eye with 5-fluorouracil, a drug which inhibits scar tissue formation, can significantly improve the success rate for glaucoma surgery. The NEI-supported multicenter trial to evaluate this study began in 1985.

SMALL GRANTS PROGRAM

Mr. Stokes. What kind of research is supported under the small grants program?

Dr. Kupfer. The NEI Small Grants Program supports pilot projects, testing of new techniques, and feasibility studies for innovative or high-risk projects.

Mr. Stokes. What is the maximum size of the award under this program?

Dr. Kupfer. This program provides one-year awards of up to $15,000 in direct costs plus indirect costs.

Mr. Stokes. Isn't the Small Grant Program particularly conducive to supporting minority scientists who are more likely to be inexperienced at obtaining NIH research grants?

Dr. Kupfer. The program is designed to support a number of types of investigators who are more likely to be inexperienced at obtaining NIH research grants. Included are: "investigators located at minority institutions."

MINORITY SCIENTISTS' PARTICIPATION IN NEI PROGRAMS

Mr. Stokes. In 1985, there were 30 small grants awarded. How many of these went to minority scientists?

Dr. Kupfer. The NEI does not maintain records on the race of investigators. However, we believe that in 1985 at least 3 small grants were awarded to minority scientists.

Mr. Stokes. What are you doing to encourage minority scientists to apply for small grants?

Dr. Kupfer. The staff of the NEI are sensitive to the need for attracting minority scientists to vision research and to biomedical research in general. Senior staff of the NEI serve on the NIH Committee on Equal Opportunity for Access in Extramural Programs and on the Coordinating Committee for NIH Minority and Women Research and Training. In addition, our health scientist administrators have been actively involved in the Extramural Associates Program serving as preceptors for a number of associates during their tenure at NIH. Our staff have visited and worked with the faculties at various Extramural-Associate institutions and worked closely with many minority investigators who have shown an interest in vision research or in any of the NEI programs.

Mr. Stokes. What is your institute doing to increase the number of minorities supported through institutional training grants that go to minority institutions?

Dr. Kupfer. The NEI staff have communicated with institutional training grant directors informing them of the NIH's commitment to attracting minority scientists to research via pre- and postdoctoral training positions. Although we do not maintain records on the race of trainees, we are familiar with a small number of successes.

Mr. Stokes. How many minorities are receiving individual fellowships through your institute?

Dr. Kupfer. The NEI does not maintain records on the race of fellows.

Mr. Stokes. In 1984, the NEI awarded $74 thousand to historically black colleges. How much was awarded in 1985?

Dr. Kupfer. In 1985 the National Eye Institute awarded $156,000 to historically black colleges.

Mr. Stokes. What are your goals for 1986 and 1987?

Dr. Kupfer. We have not set numerical goals for awards to historically black colleges. However, we support several projects in the Division of Research Resources' Minority Biomedical Support program, and in 1985 we spent $238 thousand for these projects. The amounts budgeted for 1986 and 1987 are $315,000 and $301,000 respectively. Another of our programs, the NEI Small Grants program, provides initial support for individuals to conduct small pilot studies that would allow them to establish a track record as researchers. With such experience minority and other scientists could go on to compete for other grant funds. Our long-and short-term goals are to urge black scientists and other minority scientists to apply for regular research project grants and increase their participation in the "mainstream" of vision research.

Mr. Stokes. Dr. Kupfer, do you establish goals for your senior administrators for addressing minority program and personnel issues? If not, why not?

Dr. Kupfer. The NEI will participate in efforts to meet the NIH goals for recruiting and career development of minority scientists and administrators. These goals are in the process of being finalized.

Mr. Stokes. How do you hold your senior officers accountable for meeting these goals?

Dr. Kupfer. The principles of equal employment are interwoven with programmatic responsibilities in the position description and performance appraisal standards of every NEI supervisor and manager.

Mr. Stokes. Please supply for the record the following information for SES, senior level administrative, and senior level professional positions. The current number of all such positions and the current number of these positions occupied by blacks.

Dr. Kupfer. At the present time NEI staff includes nine Senior Executive Service (SES) executives and scientists. None of the nine positions is occupied by a black at this time. A complete analysis is shown in the following table.

Pay Plan	Total Positions	Number Incumbered by Blacks
Senior Executive Service.	9	0
Senior Professional (GS/GM 14-15) . . .	25	0
Senior Administrative (GS/GM 14-15) . .	2	2
Total.	36	2

TECHNOLOGY TRANSFER ACTIVITIES

Mr. Early. Among the Institute's research programs is one in the area of technology transfer. Would you briefly describe this program and highlight some of the major research activities being supported in this area?

Dr. Kupfer. At the National Eye Institute, technology transfer encompasses a broad range of research and other activities principally conducted in the United States and to a much lesser extent abroad. Some major technology transfer programs include: the NEI's clinical trials program, knowledge transfer activities, and international blindness prevention research.

The NEI is currently supporting 28 clinical trials. In the typical multicenter clinical trial, teams of investigators at medical centers throughout the United States thoroughly familiarize themselves with the new technology to be evaluated, patients with a specific eye disease are treated, safety and efficacy data are gathered over a period of years, and the data carefully analyzed. Among the eye diseases currently under investigation in NEI-supported clinical trials are: diabetic retinopathy, retinopathy of prematurity, glaucoma, uveitis, aging-related macular degeneration, cataract, amblyopia, and retinitis pigmentosa.

When data obtained from these clinical trials yields important information about the sight-saving potential of the new techniques undergoing evaluation, the results are systematically communicated to the vision research community, to clinicians responsible for treating eye disease, and to the general public when appropriate. The NEI plans and implements numerous knowledge transfer activities in this regard, including the following: publishing the research results in medical and scientific journals, arranging for media coverage of the results, preparing public health education materials, scheduling continuing medical education courses, holding workshops and symposia, and collaborating with the private sector on information dissemination.

In an effort to transfer technology and the benefits of biomedical research to the peoples of other nations as well, the NEI collaborates with several international organizations working to prevent and treat blindness worldwide. For example, the NEI and the Indian Council of Medical Research have developed a collaborative program of blindness research under the 1983 Indo-U.S. Science and Technology Initiative. In 1985, the NEI and the Italian Ministry of Health signed an agreement to encourage cooperation in biomedical research.

Mr. Early. Is this primarily an intramural or extramural program?

Dr. Kupfer. It is primarily supported by extramural grants and contracts but both intramural and extramural research programs are involved in technology transfer activities.

Mr. Early. What level of resources were allocated for this program in FY 85? What are your estimates for FY 86 and FY 87?

Dr. Kupfer. In 1985 the Institute obligated approximately $21.4 million for these activities. Far and away the major portion of this funding--$21.3 million--was for clinical trials. International activities were funded primarily by other federal agencies and by the governments of the countries involved. Their contributions have not been enumerated here. We will spend approximately $20 million for these activities in 1986 and $22 million in 1987.

Mr. Early. Do you have any new research initiatives in this area planned for FY 87?

Dr. Kupfer. The 1987 budget request does not include any new initiatives in this area.

IMPACT OF NEW TECHNIQUES IN BIOMEDICAL SCIENCE ON EYE RESEARCH

Mr. Early. Over the past several years a number of new techniques in biomedical science have emerged. Please describe the impact some of these techniques have had on the field of eye research.

Dr. Kupfer. In particular, new techniques in three areas of science have had a profound influence on eye research. These areas are molecular genetics, immunology, and neurobiology.

MOLECULAR GENETICS

New discoveries in the field of molecular biology have led to an explosive development of techniques that are revolutionizing many aspects of biological science, medicine, and industry. Through molecular biological research, it is becoming possible for the first time to relate visual processes directly to gene processes.

Recombinant DNA techniques have become firmly established in the analysis of the visual system. These new methods may ultimately enable detailed understanding of the molecular basis for the development, functional organization, and expression and regulation of genetic information of the eye and visual system. Many eye disorders--for example, certain types of cataracts, retinal degenerations, color vision defects, and retinoblastoma--are known to be hereditary. The identification and localization of the underlying genetic defects in these disorders present scientific opportunities of high priority.

Recombinant DNA techniques are being used to study the gene families that produce structurally and functionally important proteins of the eye, such as the crystallins (lens proteins responsible for transparency), opsins (retinal proteins responsible for the visual signal), and collagens (extracellular proteins that control the shape and structure of the eye). Genes for eye crystallins and collagens already have been cloned, and the genes for the retinal protein rhodopsin are now being isolated, spliced into bacterial DNA, and produced in large quantity by growing the bacteria that carry the spliced genes. After isolation from the bacteria, the gene copies will be used in a variety of experiments to examine the activity and structure of genes in normal and diseased eyes and to discover the genetic basis for hereditary disorders in ocular tissues.

These techniques have already made it possible to demonstrate that crystallin gene expression is severely depressed in hereditary and diabetic cataracts. A type of hereditary mouse cataract has been directly associated with a defect in the expression of one specific member of the beta-crystallin gene family. Additional research should explain how and why this gene expression is depressed and may ultimately provide a means of altering the condition.

In general, recombinant DNA technology has greatly accelerated the pace of vision research and has allowed determination of the primary structures of major and minor eye proteins. Without this technology this essential information would take many years to obtain. Recombinant DNA technology also provides unusually sensitive methods to quantify and localize gene activity within the eye. Molecular genetic analysis of the visual system thus contributes enormously to our basic knowledge of the normal eye and to the molecular nature of visual disease. Moreover, current studies are bringing us closer to the time when it will be possible to prevent or correct genetic defects that cause hereditary eye disease.

IMMUNOLOGY

Major advances and the development of many new concepts and discoveries about how the body responds to infection and injury, as well as the nature of autoimmune disorders, hold great potential in the field of vision research.

Studies of the immunologic and bioregulatory aspects of vision and ocular disease may ultimately enable detailed understanding of how the various cells within the eye communicate. Regulation of organ systems by soluble proteins and cell surface receptors is now recognized as a major way in which the body controls many of its functions. The identification and localization of the underlying regulatory system in certain eye diseases, such as retinitis pigmentosa, present scientific opportunitites of high priority.

The expanding development and use of monoclonal antibodies is playing an important role in basic studies of the visual system and also is likely to be clinically useful in the long term. Because the various visual system cell types differ structurally and specific cell types undergo major structural changes during development, monoclonal antibodies permit one to examine, for example, the changes in cellular structure that occur during optic nerve development and to distinguish among the various cell types in the visual system. The ability of monoclonal antibodies to seek out and bind to specific kinds of cells may some day be used to guide drugs to specific target cells for treating certain eye disorders such as glaucoma or ocular tumors.

Ocular infection can be caused by a diverse array of infecting organisms; the special environment of the eye provides unusual opportunities for these organisms to proliferate and destroy tissue. Certain ocular structures, such as the cornea, lens, and vitreous, do not normally have blood vessels, and this decreases their immune response to foreign substances, producing desirable results, when the substance is transplanted tissue, or undesirable effects during viral, bacterial, or fungal infections. Abnormal functioning of the immune system may be an important factor in the development and spread of eye cancers, including retinoblastoma.

HERPES SIMPLEX VIRUSES

Some infecting agents can become latent and lie dormant in tissues of the body for weeks, months, or years before expressing their infective nature. For example, herpes simplex viruses (HSV) can become dormant in nerve tissue behind the eye and then be stimulated to become active again, often in response to some physical stress, such as a fever or other illness. In this dormant state, the viruses cannot be eradicated by any medications now available.

Herpes simplex virus infection of the cornea is responsible for most corneal blindness in this country. Although the initial infection may subside after treatment, nearly 25 percent of those infected experience a recurrence of the epithelial disease or a complication of the infection in the stromal layer of the cornea within two years of the initial infection. Several NEI-supported studies are designed to elucidate the mechanisms involved in the progression of HSV keratitis into latency or dormancy and the eventual reactivation of latent virus responsible for the recurrent disease.

These studies include characterization of the viral genome during latent and reactivating infection and elucidation of the complex interaction between viral antigens and the host immune response during latency and reactivation. These studies should provide information which will be useful in designing therapeutic interventions to prevent the recurrent disease.

The feasibility of producing a HSV vaccine is also under investigation. This study is testing the hypothesis that infection of the trigeminal ganglia, a group of nerve cells known to harbor the latent virus, with a live, attenuated or inactivated form of the virus will prevent secondary infection by the virulent form of the virus.

An improved method for delivery of antiviral drugs to the site of HSV infection is also being evaluated. Liposomes containing a variety of antiviral drugs which have specific antibody against HSV on the surface are being constructed. These immunoliposomes should attach specifically to virus infected cells and allow the drug to diffuse out creating a high local concentration for a prolonged period. This should inhibit viral replication close to the attachment site and reduce the required frequency of topical administration of medication required for effective treatment.

Several investigators are currently involved in the characterization of the role of autoantigens--substances within the body's tissues that act like foreign invaders and provoke an immune response--in chronic corneal, retinal, and choroidal inflammatory disease. These studies have suggested that several such antigens in the retina, retinal pigment epithelium, choroid, and optic nerve may be responsible for the autoimmune intraocular inflammation known as uveitis.

UVEITIS

About 10 percent of all visual impairment in the United States is caused by uveitis, which is an inflammation of the inner eye. Studies conducted at the NEI have shown that many cases of uveitis are autoimmune in origin. That is, they arise because the immune system has mistaken eye tissues for foreign invaders and has mounted an attack against them. Because uveitis often can't be controlled by the corticosteroids and other drugs that are generally used to treat it, the NEI recognized that there was a great need to evaluate cyclosporine as a possible agent for suppressing the abnormal immune activity that underlies many cases of this disease. At the NEI, studies conducted with animals have shown that cyclosporine can completely block the development of autoimmune uveitis and prevent blinding eye damage. Studies involving patients are still in progress.

NEI-supported researchers are testing various other anti-inflammatory agents for their safety and efficacy against ocular infections and inflammations. These include antiviral agents, various steroid compounds, and interferon.

Because corneal immune rejection is a leading cause of failure in corneal transplantation, research is currently aimed at gaining an understanding of the rejection process and attempting to modify or eliminate it. Donated corneas that have been soaked in a solution containing antibody against the histocompatibility or human lymphocyte antigens (HLA) found on the surfaces of most tissues have been shown to have an increased survival time when compared to unsoaked grafts.

The immunologic basis for this protection of donated corneas by soaking in antibody solution and the biological characteristics of the histocompatibility antigens on the surface of the cornea are currently being studied. The effect of HLA matching of donor corneas with recipient tissue on the outcome of the allograft is also being evaluated in a multi-center clinical trial.

A number of researchers are using immunochemical and biochemical techniques to study lens components in normal and pathological states. These studies include characterization of the zonular fibers--the elastic fibers which support the lens. Investigation of the normal state of these fibers will provide valuable information on the abnormal conditions which lead to lens dislocation and pseudoexfoliative syndrome, a condition in which a flaky translucent substance is deposited in the lens capsule.

Thus, research on ocular immunology is making a major contribution to the improved prevention and treatment of a variety of blinding and disabling eye conditions.

NEUROBIOLOGY

More is known about the role, structure, and physiology of the rod and cone cells of the retina than about any other type of cell in the nervous system. For example, in the past few years exciting advances have been made in clarifying the molecular events that control visual excitation--the electrochemical response of the retina to light--and adaptation--the retina's ability to alter its sensitivity to various levels of light. Much of this research has focused on the roles of light-dependent interactions of the visual pigment rhodopsin with other biomolecules in the rod cell outer segment.

The ability to monitor electrical activity in single isolated photoreceptors, to isolate "patches" of cell membrane to determine their physiological properties, and the development of ion-sensitive dyes as indicators of intracellular calcium levels (calcium is believed to be one of the excitatory transmitters released by rhodopsin), are exciting advances in neurobiological techniques which may yield large dividends. If ions and molecules thought to be involved in phototransduction are perfused into this isolated cell, the cell's response to those ions can then be measured. This new technique has opened the way for a wide range of studies of the retinal excitatory and adaptation mechanisms.

In another area of research, molecular factors are being explored that play a role in the development and function of those portions of the brain that are involved in vision. The organization of the brain is being studied at the molecular and cellular levels in an effort to discover the interactions between visual processing, visual perception, and visually guided eye movements. Investigators are studying the vestibular system and examining the neural basis of sensory and motor interactions in rhesus monkeys. The multifaceted research approach includes behavioral studies of normal monkeys, single cell recordings, studies of the neural circuitry and the anatomical connections between cells of a system, as well as assessments of the effects of discrete lesions on eye movements.

Research findings from the monkey studies are guiding tests in normal humans and in patients with deficits in the oculomotor system. In addition, an effort is being made to correlate data on human oculomotor deficits with what is known from research with monkeys. Furthermore, more accurate measurements of normal and abnormal eye movements are being obtained to learn more about how the systems function.

In Science and Technology: A Five-Year Outlook, the National Academy of Sciences, predicted that by the 21st century, neuroscience may well be the dominant science. A central issue in this field is the analysis of sensory information and its interaction with motor responses. More is known about the visual sensory and oculomotor systems than about any other neural system. The visual sensory and oculomotor systems are closely linked to one another, which is a distinct advantage from a research point of view. The visual system is the preeminent sensory system in humans, and over half of a monkey's brain is devoted to visual analysis. Similarly, the oculomotor system provides a simple, straightforward system that has many research advantages compared to other motor systems. Insights gained from such research are expected to have great practical significance in the improved prevention, diagnosis, and treatment of such disorders as strabismus, amblyopia, and nystagmus.

VISION PROBLEMS IN SCHOOL CHILDREN

Mr. Early. In reviewing your budget justification I was surprised to see that one out of every four school children in the U.S. has a vision problem. Is this high--compared to other countries? Do we know why so many children have vision problems and what the cause is?

Dr. Kupfer. The apparently high estimate of vision problems among children in the United States is in part due to our rather efficient screening programs for detecting vision problems in school age youngsters. In fact, because of the generally better nutritional and health care status of our children, they do not suffer from the vitamin deficiency or parasitic infection sources of blindness that plague much of the Third World. Nevertheless, a large number of children have less than perfect vision and require treatment or optical correction. The largest cause of poor vision in children is, of course, refractive error. By the middle of the adolescent years, as many as a third of all children show significant myopia. Other major causes of vision problems include amblyopia (lazy eye), eye movement disorders, hereditary retinal degenerations, and retinopathy of prematurity.

Mr. Early. What research initiatives are currently underway to address this problem?

Dr. Kupfer. The NEI is currently supporting a program of both basic and applied research on the causes of myopia. This research is aimed simultaneously at discovering the pathophysiological mechanisms involved in too much elongation of the eye during its growth and the hereditary and/or environmental determinants of this abnormal growth. Research in this program employs both animal models of myopia and human volunteers.

Research on amblyopia is also proceeding with both human and animal projects. We are increasing our knowledge of the different reasons that the brain "turns off" information coming from one eye, thus making it less effective or even blind. We are also learning that loss of ability to read eye charts (visual acuity) may be only one manifestation of the total deficit in amblyopia. Such understanding will be critical to our ability to treat this disorder more effectively.

As you may know, retinopathy of prematurity is once again becoming a major problem. Neonatal intensive care has resulted in more infants of very low birth weight surviving than in previous years, and the extreme immaturity of their retinas appears to make them susceptible to developing retinopathy even without excessive oxygen. The NEI has just begun a new clinical trial, involving 25 centers across the United States, to assess the value of cryotherapy (freezing some of the delicate retinal tissue) in preventing the development of blinding retinopathy in these tiny infants.

Mr. Early. Do you plan any new initiatives in this area for FY87?

Dr. Kupfer. The 1987 budget request does not include any new initiatives in this area.

CORNEAL TRANSPLANTATION

Mr. Early. The budget justification notes that corneal transplantation has the highest success rate of all tissue transplant operations. Can you tell us to what extent and why, the success rate is better here?

Dr. Kupfer. Blood vessels carry components of the immune system which can participate in graft rejection. The relative lack of blood vessels in the cornea contributes to a high success rate for corneal transplantation. Added to this built-in biological advantage have been other important factors such as 1) the skills of the transplant surgeons and 2) research advances that have led to improvements in the storage of donor corneal tissue and to the development of better suture materials and Because of these factors, tissue rejection from corneal transplantation occurs in only about 10% of surgical cases. However, if the patient's corneal bed is densely vascularized prior to surgery, rejection can lead to graft failure in up to 65% of cases. A multicenter clinical trial is being conducted now to determine whether histocompatibility antigen matching between donor and recipient will improve graft outcome in these high-risk cases.

NATIONAL VISION RESEARCH PLAN

Mr. Early. Thus far, Doctor, to what extent has NEI been able to meet the goals and objectives of the National Vision Research Plan? And how much more progress, if any, will you be able to make given your FY87 budget request?

Dr. Kupfer. On the whole, I believe that we have been very successful over the past few years in supporting research related to most of the goals and objectives specified at various levels of our National Plan. More to the point, in several research categories designated in the Plan as Program Development Priorities, we have not only made significant progress in funding additional research and gaining better understanding of fundamental processes, we actually have obtained important new information that has been of direct benefit to those suffering from blinding eye diseases. Examples of the latter include clinical trials which have demonstrated the value of laser treatment of early stage diabetic retinopathy, one type of aging-related macular degeneration, and ocular histoplasmosis. Our Plan's goal of expanding research in ocular immunology has been very well met as has that of applying new techniques in molecular biology to a wide variety of visual system problems. Progress in both areas has been rapid.

With regard to the 1987 budget, one of the most attractive features of our Plan is that it specifies in considerable detail areas of research that are both adequately funded at present and those which warrant additional funding because they represent not only great unmet needs but offer new opportunities for productive research to meet those needs.

In the course of the normal funding cycle, there will be a turnover of grants in both categories; thus, new ideas are constantly infused into both what we have identified as the Program Base and the Program Development Priorities. This will occur at both high and low funding rates because our primary criteria for funding any grant proposal is its scientific merit as judged by peer review.

But, we also employ a mechanism to help assure that important new proposals for research in areas specified in the Plan as Program Development Priorities do not fall by the wayside just because of the necessity to restrict funding in a given year. Such projects are often identified through ongoing staff review of all proposals to determine those which may have "High Program Relevance," that is, hold great promise of fulfilling one of the Plan's Priorities, especially one in which no or few grants have yet been awarded. Projects so identified are singled out and brought to the special attention of the National Advisory Eye Council. Alternatively, individual Council members may themselves identify such projects. In either case, after the Council has deliberated on these proposals, those they designate as having High Program Relevance are recommended to the NEI as deserving of special consideration for funding. This process is used sparingly, but it is used when needed.

Thus, our Plan helps us in times of both expanded and constrained budgets in keeping on our course of supporting not only the most scientifically meritorous research but that which is also most relevant to fulfiling the mission of the National Eye Institute: to improve the visual health of the American people.

IMPACT OF COMPETING PROJECT GRANT REDUCTION

Mr. Early. The FY 87 budget request would fund 250 new and competing grants, 108 fewer than the FY 86 level (pre-or post-sequestration) and 117 less than FY 85. What impact will this have on your research programs?

Dr. Kupfer. The reduction in the number of competing projects that would be funded in 1987 will mean that certain initiatives may be delayed to permit funding of new grants in areas of higher priority and to optimize support for ongoing projects.

Mr. Early. What areas of research would be affected by this reduction?

Dr. Kupfer. Some individual project in the following areas of research might be affected by these reductions:

o Development of new animal models of diabetic retinopathy and other retinal diseases that involve growth of new, abnormal blood vessels.

o Use of recombinant DNA technology to acquire information needed to improve the treatment of ocular herpesvirus infections and develop a means of preventing recurrences.

o Research to identify the causes of chronic blepharitis and associated corneal conjunctivitis and develop effective treatments.

o Research on the cornea to better understand the physical and biosynthetic factors that play a role in determining the effectiveness and predictability of the various refractive surgical procedures.

o Use of molecular biology and associated techniques to learn more about the lens and develop means of modifying its genetic makeup so as to eventually be able to prevent cataract formation.

o Research to develop non-invasive methods for continuously measuring intraocular pressure. Such tools are required for understanding the cause and progression of glaucoma.

o Application of molecular genetics to the study of glaucomas that occur early in life, in particular primary congenital glaucoma.

o Development of improved treatments for amblyopia that may give the patient a better chance of achieving normal binocular vision.

o Epidemiological studies of risk factors for myopia, clinical trials of treatments for myopia, and research on the influence of refractive and accommodative states on the development of the eye.

NEGOTIATION OF PROJECT GRANTS

Mr. Early. The budget justification states that there will be downward negotiations of 11.6% and 11.8% in competing and noncompeting grants, respectively. Will each grant be reduced by these amounts, or are these averages?

Dr. Kupfer. These are averages. NEI staff will review each application carefully to assure that no one grant would be reduced so much that the scientific integrity of the project might be jeopardized. The staff review will include an evaluation of such factors as the programmatic priority of the project, the scope of the work, the magnitude of the program, and the ability of the investigators to achieve the scientific purposes of their projects with more modest staff and resources.

Mr. Early. What effect will these reductions have on research projects? Will the scope be curtailed--research delayed?

Dr. Kupfer. As I noted above, the effect on individual projects will be minimized. Of course to achieve an average reduction some projects will bear larger reductions than others. The best investigators, working on projects in the highest priority areas, will be able to continue their work with little impact. Some projects, in contrast, will have to proceed at a slightly slower pace.

Mr. Early. Doctor, as a professional, are you concerned about the effect these large direct cost cuts will have on the ability of researchers to carry out their projects? On the quality of the research?

Dr. Kupfer. Productivity in biomedical research, as in most areas of knowledge development, requires careful nurturance. Under ideal circumstances, unlimited resources may be provided for every meritorious project. In the face of current constraints, however, priorities must be set amongst the meritorious projects in determining how resources for vision research are to be allocated. I am certain that we will be able to attack those areas identified as the highest priorities in *Vision Research: A National Plan-1983-1987* with minimal disruption from these reductions.

Mr. Early. In your professional opinion, at what point do we reach the "danger zone" -- what size cut?

Dr. Kupfer. We are close. But, once again, my staff will be considering each individual grant and will work closely with affected investigators to ensure that the scientific integrity of no project be jeopardized.

CLINICAL TRIALS

Mr. Early. Will you be able to start any new clinical trials in FY 87?

Dr. Kupfer. No, I do not believe we will be able to start any new clinical trials in 1987.

Mr. Early. Doctor, will you have to curtail any ongoing clinical trials with your FY 87 budget request? If so, which ones?

Dr. Kupfer. Since most of our clinical trials are funded as research project grants, funding amounts may be adjusted to reach the budgeted negotiation levels. However, we will provide the funds needed to continue all ongoing clinical trial awards.

Mr. Early. Are there any high priority clinical trials which are ready but cannot be initiated because of lack of funds in the FY 87 request? If so, please provide a list of these, along with a brief description and the associated costs, including first year cost.

Dr. Kupfer. The following clinical trials will be delayed in 1987:

Central Retinal Vein Occlusion Study - The central retinal artery and central retinal vein are the primary vessels through which blood enters and leaves the retinal vasculature. Occlusion of the central retinal vein (CVO) results in a shut-down of blood flow in the eye, macular edema, hemorrhage within the retina, and thrombolytic glaucoma. CVO is one of the major blinding retinal diseases. People with diabetes or hypertension are particularly at risk. There is no effective treatment and the prognosis for vision is grave. In this study, the potential of a laser technique already known to be effective in treatment of macular edema associated with branch retinal vein occlusion or with early diabetic retinopathy will be evaluated.

Duration	5 years
First Year Cost	$1,000,000
Total Cost	$5,000,000

Treatment of Optic Neuropathy with Steroids - The patient with optic neuritis experiences a sudden reduction in visual acuity and loss of central vision. Approximately 10,000 young Americans experience this disorder each year. A proportion of these people may also have signs of multiple sclerosis. Vision in most patients appears to improve over time, but it has been thought that steroid treatment advances the rate of improvement. This study will document the natural history of this disorder, evaluate the efficacy of steroid treatment, and study various deficits in visual function associated with swelling of the optic nerve, which may still be affected even after visual acuity improves.

Duration	5 years
First Year Cost	$1,500,000
Total Cost	$8,000,000

Surgical Reattachment of the Retina in Advanced Severe Retinopathy of Prematurity - About five percent of the very low birthweight infants who survive each year go on to develop severe retinopathy of prematurity (retrolental fibroplasia). Of these severe cases, many go on to retinal detachment and blindness. A number of clinical investigators have been developing a surgical procedure for reattaching the retina in these unfortunate instances. The risks and benefits of this approach will be ready for evaluation through clinical trial in 1987.

Duration	7 years
First Year Cost	$3,000,000
Total Cost	$12,000,000

Evaluations of Epikeratophakia and Keratoprostheses Treatment for Corneal Disorders - Epikeratophakia is a procedure in which a cornea obtained from a donor is lathed to optical specifications and sutured to the recipient patient's cornea to improve the resolution of the eye. This procedure has great potential benefits for patients with corneal diseases, such as those with a blinding condition called keratoconus and to other patients whose vision after cataract surgery cannot be easily corrected with other methods. In these studies, the safety and effectiveness of epikeratoprostheses will be evaluated.

Duration	5 years
First Year Cost	$1,500,000
Total Cost	$7,000,000

Surgical vs. Laser Management of Advanced Glaucoma - Until recently, glaucoma specialists have used a surgical procedure (trabeculectomy) in attempting to reduce intraocular pressure in patients who do not respond to glaucoma drug therapy. Laser procedures have recently been developed to replace this surgery. However, the relative benefits (or risks) of the two procedures are not known and this multicenter study will determine the circumstances under which each is to be preferred.

Duration	5 years

First Year Cost	$1,000,000
Total Cost	$5,000,000

Mr. Early. Will this budget request enable NEI to undertake any new initiatives?

Dr. Kupfer. No major new initiatives are planned at this time, but, we will be able to continue those areas of highest priority. The following projects are just a few examples of important ongoing research that will be emphasized in 1987.

Glaucoma - The NEI has had as a research priority epidemiologic studies to verify and possibly explain a suspected high rate of glaucoma in blacks. Now a complex research study to address this problem is underway. The research team will be supported 100% to insure that the infrastructure required for this study remains in place and the study is completed in a timely fashion.

Aldose Reductase - As the Director of NIH reported in his opening statement, the role of aldose reductase in the complications of diabetes is one of the most important questions in diabetes research. The NEI is on the threshold of developing the answer to this and many other questions about aldose reductase inhibitors. Support for developing this exciting area of research will be limited only by the availability of quality ideas and people with the skills to carry them out.

Cataract - NEI-supported research of the past sixteen years has led us to the brink of understanding why cataracts form, how, and where the critical action sites for lens changes are located. This research opportunity should be pursued to the fullest so that preventive methods of dealing with this major cause of blindness can be developed.

USE OF ADDITIONAL FUNDS

Mr. Early. If an increase over the FY 87 request is provided, how would you use these additional funds?

Dr. Kupfer. An increase over the 1987 request would make it possible for the Institute to initiate new clinical trials, restore proposed reductions due to negotiation of research project grants and core grants, and fund additional competing research project grants.

Mr. Early. Will any significant new research initiatives or opportunities be lost or delayed by lack of funds in the FY 87 budget? Please provide, for the record, a list of these along with a brief description and the funding requirements associated with each.

Dr. Kupfer. Progress in the following research areas would be delayed as a result of the current budget proposals:

o Development of new animal models of diabetic retinopathy and other retinal diseases that involve growth of new, abnormal blood vessels.

o Use of recombinant DNA technology to acquire information needed to improve the treatment of ocular herpesvirus infections and develop a means of preventing recurrences.

o Research to identify the causes of chronic blepharitis and associated corneal conjunctivitis and develop effective treatments.

o Research on the cornea to better understand the physical and biosynthetic factors that play a role determining the effectiveness and predictability of the various refractive surgical procedures.

o Use of molecular biology and associated techniques to learn more about the lens and develop means of modifying its genetic make-up.

o Research to develop a non-invasive method for continuously measuring intraocular pressure.

o Application of molecular genetics to the study of primary congenital glaucoma.

o Development of treatments for amblyopia that may give the patient a better chance of achieving normal binocular vision.

o Epidemiological studies of risk factors for myopia, clinical trials of treatments for myopia, and research on the influence of refractive and accommodative states on the development of the eye.

Enhanced research in these areas would cost approximately $6-8 million in 1987.

IMPACT OF 1987 BUDGET LEVELS

Mr. Early. Doctor, will any significant research initiatives currently underway be halted or seriously delayed due to FY 87 funding levels?

Dr. Kupfer. The 1987 funding levels would affect ongoing research, as well.

Mr. Early. To what extent will there be major reductions in the scope of ongoing or new initiatives because of the FY 87 funding levels?

Dr. Kupfer. Approximately 25 percent of NEI research project grants will terminate in 1986 and must recompete for support in 1987. Historically, almost 100 percent of these will compete successfully and be eligible for funding in 1987. Since the projected award rate for NEI is 36 percent in 1987 as compared to 50 percent in 1986, a significant number of these competing renewal applications will not be fundable and the projects will be phased out or terminated.

Mr. Early. For the record, please provide a list of these along with a brief description and the amounts associated with each initiative.

Dr. Kupfer. Until all grant applications are received and reviewed, it is difficult to list specific projects that will not be funded. The following are examples of ongoing activities would be affected:

o Studies of the metabolism of the cells that line the small blood vessels of the retina. $450,000

o Training more investigators in the tissue culture methods needed for detailed studies of these retinal vascular cells. $150,000

o Studies of specific aspects of the immune-mediated inflammatory response that occurs in the potentially blinding, parasitic disease onchocerciasis. $150,000

o Improvement of methods to evaluate the permeability of the cornea, and other aspects of corneal membrane function, in the living eye. $300,000

o Research on normal corneal development, utilizing cultures of the major types of corneal cells, and monoclonal antibodies developed to label specific corneal components. $150,000

o Genetic studies of families with hereditary cataracts to allow analysis of these diseases at the gene level and improve understanding of human cataracts. $220,000

o Studies to learn more about the composition and development of the zonular fibers that hold the lens in place in the normal eye, by biochemical analysis of the fibers and by improving techniques for the culture of the cells that the fibers attach to. $150,000

o Use of fluorophotometry to better measure inflow and outflow of aqueous humor in the eyes of primates, and thus further our ability to evaluate the effects of drugs in normal and glaucomatous eyes. $170,000

o Development and characterization of anti-glaucoma drugs designed specifically to act on the tissues that play a role in the outflow of aqueous from the eye. $100,000

o Development of better tests and analytic strategies for diagnosing and treating glaucoma. $220,000

o Use of molecular biological techniques to study the anatomical and physiological mechanisms underlying amblyopia and other effects of visual deprivation. $420,000

o Research on the function of synaptic transmitters in the nerve cells of the visual portion of the central nervous system. $280,000

o Research on drug treatments for strabismus. $180,000

CORE AND CENTER GRANTS

Mr. Early. The budget indicates that direct costs for competing research centers will be reduced by 20% in FY 87. Are reductions of this size something we need to be concerned about?

Dr. Kupfer. The proposed reductions can be accommodated in the short term.

Mr. Early. What effect will these cuts have on the research programs at these centers?

Dr. Kupfer. NEI core center grants for vision research provide centralized research resources for groups of vision researchers who have already competed successfully for independent research grant support. The centralized resources are targeted at enhancing the overall research capability of the group, but are not intended to supplement individual research efforts alone. Thus, reductions in this area will not impact on individual research projects but will be expressed in the form of limited resources for collaborative projects.

NEI specialized clinical research centers provide resources for coordinated sets of studies on a specific ocular disorder in human patients. We do not anticipate any competing applications for this type of center grant in 1987.

Mr. Early. How will the reduction in the size and scope of the centers program affect NEI's program plans--both immediate and long range?

Dr. Kupfer. In *Vision Research -- A National Plan: 1983-1987*, the National Advisory Eye Council reaffirms the position that the NEI should give priority "...to individual research project grants, each competing on its own merits," rather than to center-type or program project grants. Thus, planned reductions in this area are higher than in other program areas.

Mr. Early. What kinds of research programs are being supported through core and center grants? Please provide a list of those grantees currently supported.

Dr. Kupfer. The Core Grants for Vision Research currently supported by the National Eye Institute are at the following institutions:

CORE GRANTS FOR VISION RESEARCH SUPPORTED BY THE NATIONAL EYE INSTITUTE

SCHOOL
Emory University
Medical College of Georgia
Johns Hopkins University
University of California, Berkeley
University of Alabama, Birmingham
Harvard University
Eye Research Institute of Retina Foundation
Massachusetts Institute of Technology
University of Illinois, Chicago
Wayne State University
Duke University
Baylor College of Medicine
Estelle Doheny Eye Foundation
University of California, Los Angeles
University of Miami
Medical College of Wisconsin
Yale University
Louisiana State University Medical Center
Mount Sinai School of Medicine
New York University
University of Pennsylvania
Oakland University
University of Rochester
Washington University
Medical Research Institute of San Francisco
University of California, San Francisco
University of Washington
Purdue University

Mr. Early. To what extent is the Institute's clinical research supported through these mechanisms?

Dr. Kupfer. The NEI's clinical research is supported primarily through cooperative agreements and contracts for multicentered clinical trials and through individual project grants. An analysis we conducted a few years ago indicated that nearly 50% of the NEI projects supported through individual research grants involved clinical research. The core grants for vision research provide core facilities for investigators involved in both basic and clinical research. Most importantly, they foster environments in which basic and clinical investigators collaborate in joint projects. They advance the rate and scope of research relevant to the prevention and treatment of disease by bringing investigators from many disciplines--basic and clinical--together to focus their efforts on the eventual eradication of eye disease.

RESEARCH CAREER PROGRAM

Mr. Early. What types of research career awards does NEI support?

Dr. Kupfer. The National Eye Institute has a small Research Career Development Award Program, as our preference has been to support outstanding younger investigators through their own individual research grant project awards. Thus, over the past few years, research career development awards have been reserved only for the most promising emerging investigators. We have at the same time, however, been actively pursuing the young clinician who is interested in developing a research career and providing support through the physician scientist award. In 1987, we will continue to emphasize the physician scientist award, and we will make fewer RCDAs.

Mr. Early. The budget request reflects a reduction in research career awards from 15 in FY 86 to 12 in FY 87. In what areas will this reduction be made?

Dr. Kupfer. We will make three fewer research career awards in 1987 because the project periods for these grants terminate with the 1986 award. Two of the recipients will continue their work with research project grant support. If the third research career award recipient demonstrates that the training which he is receiving now is successful, his research proposal will be supported also in 1987.

Mr. Early. I recall, NEI supported 20 and 13 Research Career Program (RCP) awards in 1983 and 1984 respectively. Doctor, is this continuing reduction in the RCP a cause for concern?

Dr. Kupfer. Yes, the number of RCP awards from the NEI has been going down over the past few years. But, no, this is not a matter of concern to us. The reduction has been due more to programmatic considerations than due to fiscal constraints.

SMALL GRANT PROGRAM

Mr. Early. What is the purpose of the small grant awards program? How would you evaluate this program?

Dr. Kupfer. The NEI Small Grant Program provides one-year awards, not to exceed $15,000 in direct costs each, for pilot projects, testing of new techniques, or feasibility studies of innovative research. The program is designed to support clinicians with limited research experience, recently trained basic scientists, investigators whose research careers have been interrupted, investigators changing fields of research, investigators located at minority institutions or at largely non-research environments, and established investigators needing quick support for a pilot project. The NEI has supported 30 to 40 of these awards over each of the past five years. We are now in the process of evaluating the successes of this program. Our initial findings have been that a number of investigators supported by this award have gone on to successfully compete for individual research grant awards based on the pilot studies supported by the small grant. In particular, we have found that the small grant is an effective mechanism for the development of research projects by MDs with minimal prior research experience.

Mr. Early. The FY 87 request proposes a 50% reduction in the number of small grant awards. Was this cut necessitated solely by fiscal constraints?

Dr. Kupfer. The NEI would reduce the number of small grant awards in 1987 to make funds available for ongoing research activities of higher priority so it reflects our priorities in times of fiscal constraint.

Mr. Early. What types of activities will be affected?

Dr. Kupfer. We will be able to fund only the best of the best proposals. Thus, the number of individuals in the target groups identified above whose pilot work we will be able to support will be reduced.

Mr. Early. What impact will this reduction have on NEI's research program?

Dr. Kupfer. This reduction will not have a major impact on the overall stability of NEI's research program, but it will limit our ability to assist various investigators in establishing the feasibility of certain innovative and high risk research projects and in establishing a basis on which to build a more extensive research program.

R&D CONTRACTS

Mr. Early. The budget request indicates you will be funding 7 more R&D contracts than in FY 86. What new activities will be supported?

Dr. Kupfer. A number of activities would be supported with additional funds included for research and development contracts in 1987. Research to better understand diabetic retinopathy will be emphasized. Also, studies to determine the risk factors responsible for the development of a wide variety of eye diseases will be expanded. Within the area of risk factor studies, priorities have been established for a number of these investigations including: studies of blindness and visual impairment from open-angle and other types of glaucoma, epidemiologic studies of macular disease, longitudinal studies of genetic cataracts, and genetic and epidemiologic studies of risk factors for strabismus. The data from these studies should reveal important information about the etiology and risk factors associated with these diseases.

Mr. Early. How will you accomplish this with an 850K increase?

Dr. Kupfer. The budget request for research and development contracts is sufficient to adequately support these activities in 1987.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

National Eye Institute

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NATIONAL INSTITUTES OF HEALTH

National Eye Institute

For carrying out section 301 and title IV of the Public Health Service Act with respect to eye diseases and visual disorders, [$195,168,000] *$179,201,000. (Department of Health and Human Services Appropriation Act, 1986).*

NATIONAL INSTITUTES OF HEALTH

National Eye Institute

Amounts Available for Obligation 1/

	1985	1986	1987
Appropriation	$181,678,000	$195,168,000	$179,201,000
Enacted administrative reduction	--	-74,000	--
Sequester order	--	-8,389,000	--
Proposed rescission	--	-5,224,000	--
Subtotal, adjusted appropriation	181,678,000	181,481,000	179,201,000
Comparative transfer to:			
Office of the Assistant Secretary for Health, for AIDS Projects	-200,000	-96,000 2/	--
National Cancer Institute for changes in the Central Services financing mechanisms and formulas	-3,087,000	--	--
Subtotal, adjusted budget authority	178,391,000	181,385,000	179,201,000
Unobligated balance, start of year	--	78,000	--
Unobligated balance, end of year	-78,000	--	--
Unobligated balance lapsing	-302,000	-101,000	--
Total obligations	178,011,000	181,362,000	179,201,000

1/ Excludes the following amount for reimbursable activities carried out by this account: 1985 -- $308,000; 1987 -- $104,000 for AIDS projects.

2/ Comparative transfer for the appropriation is $100,000.

National Eye Institute

Budget Mechanism
(Dollars in Thousands)

	1986 Appropriation 1/2/ No.	1986 Appropriation 1/2/ Amount	1986 Available after Sequestering 1/3/ No.	1986 Available after Sequestering 1/3/ Amount	1986 Revised 1/3/ No.	1986 Revised 1/3/ Amount	1987 No.	1987 Amount
Research grants:								
Research projects								
Noncompeting	783	$101,469	783	$97,106	783	$95,072	853	$101,642
Admin. supplemental	(45)	880	(45)	842	(45)	842	(38)	1,750
Competing								
Renewal	171	26,500	171	25,360	158	23,602	119	19,090
New	185	20,486	185	19,608	171	18,176	129	14,699
Supplemental	2	80	2	78	2	78	2	80
Subtotal, competing	358	47,066	358	45,046	331	41,856	250	33,869
Subtotal, research projects	1,141	149,415	1,141	142,994	1,114	137,770	1,103	137,261
Research centers	29	6,100	29	5,838	29	5,838	29	5,400
Other Research								
Research career program	15	887	15	849	15	849	12	625
Small grants	30	713	30	683	30	683	15	350
Minority biomedical support		315		301		301		301
Other Research related	5	463	5	442	5	442	5	500
Subtotal, other Research	50	2,378	50	2,275	50	2,275	32	1,776
Total, Research grants	1,220	157,893	1,220	151,107	1,193	145,883	1,164	144,437

Training								
Individual awards								
Noncompeting....................	72	1,745	72	1,669	72	1,669	67	1,645
Competing.......................	36	870	36	834	36	834	31	743
Subtotal, individual awards...	108	2,615	108	2,503	108	2,503	98	2,388
Institutional awards								
Noncompeting....................	92	2,216	92	2,121	92	2,121	85	2,210
Competing								
Renewal........................	8	400	8	383	8	383	7	178
New............................	--	--	--	--	--	--	--	--
Subtotal, institutional.......	100	2,616	100	2,504	100	2,504	92	2,388
Total, training....................	208	5,231	208	5,007	208	5,007	190	4,776
Research & development contracts....	48	6,649	48	6,363	48	6,363	55	7,215
					FTEs		FTEs	
Intramural Research.................		16,051		15,360	140	15,360	140	16,723
Research management and support.....		5,948		5,591	63	5,591	63	6,050
Construction........................		3,300		3,158		3,158		--
TOTAL............................		195,072		186,586	203	181,362	203	179,201

1/ Reflects an enacted administrative reduction of $74,000 and a carryover in unobligated funds of $78,000.

2/ Reflects a comparable transfer of $100,000 to the Office of the Assistant Secretary for Health for AIDS projects.

3/ Reflects a consultant services (Section 515 of the Treasury-Postal Service Appropriation Act, 1985) withholding of $101,000 and a $96,000 comparable transfer to the Office of the Assistant Secretary for Health for AIDS projects.

NATIONAL INSTITUTES OF HEALTH

National Eye Institute

CROSSWALK - 1986 Appropriation 1/

(Dollars in Thousands)

PROGRAM ACTIVITY	MECHANISM Research Grants Research Projects	 Research Centers	 Other Research	 Training Programs Individual	 Institutional	 Research and Development Contracts	 Intramural Research	 Research Management and Support	 Construction	 Total
Retinal and choroidal diseases	$61,402	$5,967	$1,195	$1,145	$942	$6,649				$77,300
Corneal diseases	26,728	---	306	341	825	---				28,200
Cataract	13,870	133	156	95	---	---				14,254
Glaucoma	15,672	---	113	45	---	---				15,830
Strabismus, amblyopia and visual processing	31,743	---	608	989	849	---				34,189
Vision Research facilities									$3,300	3,300
Intramural Research							$16,051			16,051
Research management and support								$5,948		5,948
Total	149,415	6,100	2,378	2,615	2,616	6,649	16,051	5,948	3,300	195,072

1/ Reflects an enacted administrative reduction of $26,000, a carryover in unobligated funds of $78,000 and a comparable transfer of $100,000 to the Office of the Assistant Secretary for Health for AIDS projects.

NATIONAL INSTITUTES OF HEALTH

National Eye Institute

CROSSWALK - 1986 Available After Sequestering [1/]

(Dollars in Thousands)

PROGRAM ACTIVITY	Research Grants			Training Programs		Research and Development Contracts	Intramural Research	Research Management and Support	Construction	Total
	Research Projects	Research Centers	Other Research	Individual	Institutional					
Retinal and choroidal diseases..............	$58,187	$5,710	$1,145	$1,094	$902	$6,363	--	--	--	$73,401
Corneal diseases.......	25,779	--	291	328	790	--	--	--	--	27,188
Cataract................	13,424	128	149	91	--	--	--	--	--	13,792
Glaucoma................	15,148	--	108	44	--	--	--	--	--	15,300
Strabismus, amblyopia and visual processing...........	10,456	--	582	946	812	--	--	--	--	12,796
Vision Research facilities...........	--	--	--	--	--	--	--	--	$3,158	3,158
Intramural Research....	--	--	--	--	--	--	$15,360	--	--	15,360
Research management and support...........	--	--	--	--	--	--	--	$5,591	--	5,591
Total.............	122,994	5,838	2,275	2,503	2,504	6,363	15,360	5,591	3,158	186,586

[1/] Reflects an enacted administrative reduction of $74,000, a carryover in unobligated funds of $78,000, a consultant services (Section 515 of the Treasury-Postal Service Appropriation Act, 1985) withholding of $101,000 and a comparable transfer of $96,000 to the Office of the Assistant Secretary for Health for AIDS projects.

NATIONAL INSTITUTES OF HEALTH

National Eye Institute

CROSSWALK - 1986 Revised Estimate 1/

(Dollars in Thousands)

PROGRAM ACTIVITY	Research Grants			Training Programs		Research and Development Contracts	Intramural Research	Research Management and Support	Construction	Total
	Research Projects	Research Centers	Other Research	Individual	Institutional					
Retinal and choroidal diseases...............	$56,014	$5,710	$1,145	$1,094	$902	$6,363	--	--	--	$71,228
Corneal diseases.......	24,844	--	291	328	790	--	--	--	--	26,253
Cataract...............	12,943	128	149	91	--	--	--	--	--	13,311
Glaucoma...............	14,579	--	108	44	--	--	--	--	--	14,731
Strabismus, amblyopia and visual processing...........	29,390	--	582	946	812	--	--	--	--	31,730
Vision Research facilities...........	--	--	--	--	--	--	--	--	$3,158	3,158
Intramural Research....	--	--	--	--	--	--	$15,360	--	--	15,360
Research management and support..........	--	--	--	--	--	--	--	$5,591	--	5,591
Total............	137,770	5,838	2,275	2,503	2,504	6,363	15,360	5,591	3,158	181,362

1/ Reflects an enacted administrative reduction of $74,000, a carryover in unobligated funds of $78,000, a consultant services (Section 515 of the Treasury-Postal Service Appropriation Act, 1985) withholding of $101,000 and a comparable transfer of $96,000 to the Office of the Assistant Secretary for Health for AIDS projects.

NATIONAL INSTITUTES OF HEALTH

National Eye Institute

CROSSWALK - 1987 Congressional Justification

(Dollars in Thousands)

PROGRAM ACTIVITY	Research Grants			Training Programs		Research and Development Contracts	Intramural Research	Research Management and Support	Total
	Research Projects	Research Centers	Other Research	Individual	Institutional				
Retinal and choroidal diseases..............	$55,009	$5,275	$1,055	$1,159	$976	$7,215	--	--	$70,689
Corneal diseases........	24,853	--	176	252	868	--	--	--	26,149
Cataract................	12,967	125	109	74	--	--	--	--	13,275
Glaucoma................	14,588	--	47	49	--	--	--	--	14,684
Strabismus, amblyopia and visual processing...........	29,844	--	389	854	544	--	--	--	31,631
Intramural Research....	--	--	--	--	--	--	$16,723	--	16,723
Research management and support...........	--	--	--	--	--	--	--	$6,050	6,050
Total............	137,261	5,400	1,776	2,388	2,388	7,215	16,723	6,050	179,201

National Eye Institute
Summary of Changes

1986 Current estimate budget authority	$181,362,000
1987 Estimate budget authority	179,201,000
Net change	-2,161,000

	1986 Base	Change from Base
Increases:		
A. Built-in:		
1. Within-grade increases	$7,357,000	+$123,000
2. Federal Employees Compensation Fund increase	25,000	+5,000
3. FTS rate increase	150,000	+46,000
4. Payment for centrally furnished services	5,105,000	+494,000
5. Increased cost of laboratory supplies, materials and other expenses	15,936,000	+334,000
Subtotal, built-in	--	+1,002,000
B. Program:		
1. Research projects:		
a. Noncompeting continuations converting from competing status	95,914,000	+38,348,000
b. Competing (new, renewals and supplements)	41,856,000	+33,869,000
2. Research centers:		
a. Noncompeting continuations converting from competing status	4,704,000	+1,112,000
b. Competing (new and renewals)	1,134,000	+592,000
3. Other Research:		
a. Noncompeting continuations converting from competing status	1,392,000	+142,000
b. Competing (new and renewals)	883,000	+480,000
4. Individual training awards:		
a. Noncompeting continuations converting from competing status	1,669,000	+766,000
b. Competing (new and renewals)	834,000	+743,000
5. Institutional training awards:		
a. Noncompeting continuations converting from competing status	2,121,000	+352,000

Summary of Changes -- continued

b. Competing (new and renewals)	383,000	+178,000
6. Research and development contracts:		
a. Continuations	6,363,000	+852,000
7. Intramural Research		
a. Program increase in high priority areas	11,468,000	+617,000
8. Research Management and Support		
a. Increase to upgrade information system	4,468,000	+203,000
Subtotal, program	--	+78,254,000
Total increases	--	+79,256,000
Decreases:		
Program:		
1. Research projects:		
a. Noncompeting completed or converted to competing status	95,914,000	-30,870,000
b. Competing completed or converted to non-competing status	41,856,000	-41,856,000
2. Research centers:		
a. Noncompeting completed or converted to competing status	4,704,000	-1,008,000
b. Competing completed or converted to non-competing status	1,134,000	-1,134,000
3. Other Research:		
a. Noncompeting completed or converted to competing status	1,392,000	-238,000
b. Competing completed or converted to non-competing status	883,000	-883,000
4. Individual training:		
a. Noncompeting completed or converted to competing status	1,669,000	-790,000
b. Competing completed or converted to non-competing status	834,000	-834,000
5. Institutional training:		
a. Noncompeting completed or converted to competing status	2,121,000	-263,000

Summary of Changes -- continued

b. Competing completed or converted to non-competing status	383,000	-383,000
6. Construction	3,158,000	-3,158,000
Subtotal, program	--	-81,417,000
Total, decreases	--	-81,417,000
Total, net change	--	-2,161,000

National Eye Institute
Budget Authority By Activity
(Dollars in Thousands)

	1986 Appropriation 1/	1986 Available after Sequestering 2/	1986 Revised 2/		1987	
	Amount	Amount	FTEs	Amount	FTEs	Amount
Retinal and choroidal diseases...............	$77,300	$73,401		$71,228		$70,689
Corneal diseases.......	28,200	27,188		26,253		26,149
Cataract...............	14,254	13,792		13,311		13,275
Glaucoma...............	15,830	15,300		14,731		14,684
Strabismus, amblyopia and visual processing..	34,189	32,796		31,730		31,631
Vision Research facilities.............	3,300	3,158		3,158		--
Intramural Research....	16,051	15,360	140	15,360	140	16,723
Research management and support............	5,948	5,591	63	5,591	63	6,050
Total obligations......	195,072	186,586	203	181,362	203	179,201
Unobligated balance, start of year..........	-78	-78		-78		--
Unobligated balance lapsing............. .	--	+101		+101		--
Total	194,994	186,609	203	181,385	203	179,201

NOTE: All 1986 columns reflect an enacted administrative reduction of $74,000.

1/ Reflects a comparable transfer of $100,000 to the Office of the Assistant Secretary for Health for AIDS projects.

2/ Reflects a comparable transfer of $96,000 to the Office of the Assistant Secretary for Health for AIDS projects.

National Eye Institute

Obligations by Object

	1985 Actual	1986 Estimate	1987 Estimate
Total number of full-time permanent positions	187	187	187
Total compensable workyears:			
Full-time equivalent employment	218	206	206
Full-time equivalent of overtime and holiday hours	1	2	2
Average ES salary	$66,232	$66,232	$66,232
Average GS grade	9.14	9.14	9.14
Average GS salary	28,224	28,224	28,224
Average salary, grades established by act of July 1, 1944 (42 U.S.C. 207)	35,361	35,361	35,361
Average salary of ungraded positions	23,206	23,206	23,206
Personnel compensation:			
Permanent positions	$5,251,000	$5,356,000	$5,430,000
Positions other than permanent	2,069,000	2,001,000	2,160,000
Other personnel compensation	196,000	200,000	205,000
Special personal services payment	308,000	320,000	335,000
Subtotal, personnel compensation	7,824,000	7,877,000	8,130,000
Personnel benefits	960,000	1,050,000	1,082,000
Benefits for former personnel	13,000	13,000	13,000
Travel and transportation of persons	361,000	430,000	455,000
Transportation of things	24,000	25,000	30,000

Obligations by Object

	1985 Actual	1986 Estimate	1987 Estimate
Rent, communications and utilities........................	667,000	700,000	750,000
Printing and reproduction.........	162,000	188,000	200,000
Other services:			
Project contracts...............	7,123,000	6,363,000	7,215,000
Centrally furnished services....	5,230,000	5,105,000	5,599,000
Other..........................	2,797,000	3,224,000	3,694,000
Supplies and materials............	1,457,000	1,445,000	1,720,000
Equipment.........................	1,332,000	894,000	1,100,000
Lands and structures..............	21,000	--	--
Grants, subsidies and contributions..................	150,040,000	154,048,000	149,213,000
Total......................	178,011,000	181,362,000	179,201,000

Significant Items Senate Appropriations Committee Report

Item	Action Taken or to be Taken
1986 Senate Report	
Vision Research Plan	
The Committee understands that the NEI's vision research plan is undergoing midcourse review. The purpose of this evaluation is to update the plan, recognizing the many new opportunities that now exist for research on eye diseases as a result of the rapid progress that has been made in applying techniques in molecular biology, immunology, and neuroscience. The Committee would like to receive a copy of the final midcourse evaluation as soon as it is published.	1. The draft of the detailed midcourse evaluation of all National Eye Institute programs is in the final stage of editing. The document will be published in April 1986 and a copy will be sent to the Committee.

NATIONAL INSTITUTES OF HEALTH
National Eye Institute

Authorizing Legislation

	PHS Act/ Other Citation	U.S. Code Citation	1986 Amt. Authorized	1986 Estimate	1987 Amt. Authorized	1987 Budget Request
Research and Investigation	Section 301	42§241	Indefinite	$176,378,000	Indefinite	$174,425,000
National Eye Institute	Section 455	42§285i	Indefinite		Indefinite	
National Research Service Awards	Section 487	42§288	244,000,000 1/	5,007,000	260,000,000 1/	4,776,000
Total Budget Authority				181,385,000		179,201,000

1/ This training authority is shared with other research training programs of the National Institutes of Health; the Alcohol, Drug Abuse, and Mental Health Administration; and the Health Resources and Services Administration.

National Eye Institute

Appropriations History

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation [1]
1978	65,436,000	85,400,000	75,352,000	85,400,000
1979	86,428,000	100,549,000	100,549,000	105,192,000
1980	104,462,000	107,528,000	113,000,000	112,989,000
1981	116,046,000	117,635,000	117,884,000	117,983,000
1982	116,445,000 [2]	132,920,000	133,014,000	127,374,000
1983	131,550,000	138,763,000	145,040,000	141,897,000
1984	142,333,000	149,600,000 [3]	151,966,000 [3]	152,262,000
1985	157,873,000	171,097,000 [4]	187,181,000	178,591,000
1985 Proposed Recission	-173,000			
1986	183,341,000	188,988,000 [5]	184,036,000	195,094,000
1986 Sequester	-8,389,000			
1986 Proposed Rescission	-5,224,000			
1987	179,201,000			

[1] Reflects enacted supplementals, rescissions, and reappropriations.
[2] Reflects the September amendment; the original request was $132,324,000.
[3] Excludes $3,585,000 in NRSA training programs not considered.
[4] Excludes $3,900,000 in NRSA training programs not considered.
[5] Excludes $5,231,000 in NRSA training programs not considered.

National Eye Institute
(Dollars in thousands)

Justification

	1986 1/2/ Appropriation Amount	1986 Available after 1/3/ Sequestering Amount	1986 1/3/ Revised FTEs	1986 1/3/ Revised Amount	1987 FTEs	1987 Amount
Retinal and Choroidal Diseases......	$77,300,000	$73,401,000		$71,228,000		$70,689,000
Corneal Diseases......	28,200,000	27,188,000		26,253,000		26,149,000
Cataract......	14,254,000	13,792,000		13,311,000		13,275,000
Glaucoma......	15,830,000	15,300,000		14,731,000		14,684,000
Strabismus, amblyopia and visual processing....	34,189,000	32,796,000		31,730,000		31,631,000
Vision research facilities....	3,300,000	3,158,000		3,158,000		--
Intramural research......	16,051,000	15,360,000	140	15,360,000	140	16,723,000
Research management and support...	5,948,000	5,591,000	63	5,591,000	63	6,050,000
Total obligations...	195,072,000	186,586,000	203	181,362,000	203	179,201,000

1/ Reflects an enacted administrative reduction of $74,000, and a carryover in unobligated funds of $78,000.

2/ Reflects a comparable transfer of $100,000 to the Office of the Assistant Secretary for Health for AIDS projects.

3/ Reflects a consultant services (Section 515 of the Treasury-Postal Service Appropriation Act, 1985) withholding of $101,000 and a $96,000 comparable transfer to the Office of the Assistant Secretary for Health for AIDS projects.

General Statement

The National Eye Institute (NEI) administers programs under authority of the Public Health Service Act to conduct and support research for new treatments and cures for blinding eye diseases and visual disorders. To meet its legislative mandate, the Institute plans, supports, and conducts a multifaceted research program. This program includes basic and clinical research, clinical trials, research training, technology transfer, and career development in the special health problems and requirements of the visually impaired and on the mechanisms of visual function and preservation of sight.

From an initial appropriation in FY 1970 of $24 million, which included support for approximately 350 individual project grants, the NEI's budget has grown to $181 million in FY 1986, which includes support for 332 investigator-initiated grants. Today, the NEI funds approximately 80 percent of all vision research supported by the Federal Government and national private philanthropic agencies combined.

In the United States, over 10 million people suffer from visual impairment that cannot be corrected by eyeglasses or contact lenses. Of these people, 1.5 million are so severely impaired that they cannot read ordinary newsprint. Vision research conducted and supported by the NEI is classified into the following five major programs that encompass basic and applied studies on the leading causes of blindness and visual disability: retinal and choroidal diseases; corneal diseases; cataract; glaucoma; and strabismus, amblyopia, and visual processing. The Institute has also established a special category of research support related to severe visual impairment and its rehabilitation.

Research project grants to individual investigators receive the highest priority at the NEI because the research they support is the primary source from which fundamental discoveries emerge. The Institute complements its research grants with a program of institutional and individual fellowships, recognizing that it takes years to nurture and develop outstanding investigators and that the level of training supported today determines our research capability in the future.

The clinical trial has become an important research mechanism for the National Eye Institute. These trials evaluate treatments for major causes of blindness and other vision disorders, to the benefit of present and future patients and their physicians.

Within its intramural program, the NEI has assembled a team of investigators who are leaders in their respective fields. The intramural research program focuses on epidemiology, clinical studies, immunology, combined laboratory and clinical approaches to neuro-ophthalmic problems, and, most recently, molecular biology.

In addition to combatting eye diseases and visual impairment in the United States, the NEI is cooperating with several international organizations working to prevent and treat blindness worldwide. Today, at least 28 million of the world's people are blind, with most of them living in the developing nations of Asia, Latin America, and Africa. At the current level of medical intervention, the number of blind people is projected to double by the year 2000. Because eighty percent of this blindness could be prevented with appropriate application of existing knowledge, or could be cured, an international effort in technology transfer to reduce this toll is underway, and the National Eye Institute is an active participant.

For instance the NEI and the Indian Council of Medical Research have developed a collaborative program of blindness research under the 1983 Indo-U.S. Science and Technology Initiative. Four research projects are underway on senile cataract, Eales' disease, detection of early vitamin A deficiency, and nutritional blindness. On March 12, 1985, the NEI and the Italian Ministry of Health signed an agreement to encourage cooperation in biomedical research. The two organizations have agreed to perform a genetic study of retinitis pigmentosa, which is particularly prevalent in Sardinia. A second project will evaluate risk factors associated with age-related cataract.

Overall Budget Policy

The 1987 budget request for the NEI of $179,201,000 is $2,161,000 below the 1986 estimate.

These levels will be achieved by limiting indirect costs and by negotiating direct costs downward. The request will support 250 competing project grants at an average cost of $135,000. This represents a 10.1 percent increase in direct costs over 1986 and a 11.6 percent reduction from full recommended levels. Historically, these reductions have averaged 3 to 4 percent. The request will support 853 noncompeting project grants at an average cost of $119,000. This represents approximately the same level for direct costs as 1986 and an 11.8 percent reduction from full commitment levels. Historically, these reductions have averaged 1 percent.

In 1987 the Institute will support 29 core and center grants at $5,400,000. Costs on these grants will be negotiated downward approximately 20 percent in order to continue funding for as many eligible institutions as possible. The rate of negotiation for these grants was 4.3 percent in 1986.

The 1987 request will provide committed amounts for the research career and minority biomedical support programs and for other research-related grants. The request also includes funds for 15 small grants.

An estimated 190 full-time-training-positions will be supported in 1987 at the same stipend levels as in 1986.

The research and development contract program includes an increase of $852,000 above the 1986 amount. Thus, the request will make it possible to continue ongoing clinical trials and to initiate another important collaborative study. Research to better understand diabetic retinopathy will be emphasized with this increment.

The 1986 budget request for the Intramural Research Program is $16,723,000, an increase of $1,363,000 over the comparable 1986 level. Funds have been included to cover mandatory cost increases. The increase also provides funds to upgrade the environment and care of research animals in response to legal requirements and to satisfy other animal welfare concerns.

The 1987 budget request for Research Management and Support is $6,050,000 an increase of $459,000 over the 1985 level of $5,591,000. This increase will allow funding for mandatory cost increases and provides funds for management improvement projects and the cyclical review of the NEI program plan.

Program Accomplishments

Hereditary disorders are responsible for one out of every five cases of blindness in the United States and account for a significant portion of the $16 billion that Americans spend each year for treatment and special services necessitated by visual disabilities. For years, medical scientists have been hampered in their efforts to find effective treatment for hereditary retinal degenerations because of the great difficulties involved in identifying the specific genetic and biochemical defects responsible for retinal breakdown in these disorders. Now, NEI-supported scientists are participating in an international effort to overcome this problem through the new techniques of molecular genetics. Scientists are employing gene probes--small bits of DNA that attach to chromosomes--as markers to estimate the location of particular genes. NEI grantees studying a rare eye tumor called retinoblastoma were the first scientists to use these molecular genetic techniques successfully in patients with hereditary eye disease.

Two NEI grantees have contributed to recent advances in locating genes for hereditary retinal degenerations. These investigators have confirmed and refined other investigators' estimates of the location of the gene for X-linked retinitis pigmentosa (RP). They are now engaged in a long-term program of research that will broaden the scope of this work to include the difficult-to-locate genes that are responsible for the more common, "autosomal" forms of RP. Part of this research will be conducted in collaboration with Italian scientists under the U.S.-Italy program for cooperation in health and medicine.

Diabetes is responsible for loss of vision in thousands of Americans each year. It is the leading cause of new cases of blindness in people 20 to 74 years of age. The NEI supports research aimed at overcoming diabetes-induced ocular problems, which are believed to affect as many as 40 percent of America's 10 to 11 million diabetics. In one NEI-supported clinical trial, the Early Treatment Diabetic Retinopathy Study (ETDRS), focal photocoagulation, a type of laser treatment, is being evaluated in patients who are still in the early stages of diabetic eye disease. Recent results from this study show that it is possible to halt or even reverse the visual loss that occurs in many people with diabetic macular edema, i.e., swelling in the small portion of the retina that provides sharp central vision. The laser treatment reduces the swelling, often preventing further vision loss and in some cases improving sight. In a study published in the American Medical Association's Archives of Ophthalmology, researchers said the laser treatment marked a significant advance in the treatment of eye problems associated with diabetes. The results of the ETDRS trial underscore the need for diabetics to get annual eye examinations to see if they need laser treatment.

There was also good news this year for diabetics who have experienced severe vitreous hemorrhage, one of the most devastating events in the progression of diabetic retinopathy. In the NEI-supported Diabetic Retinopathy Vitrectomy Study (DRVS) two approaches to surgical restoration of sight were compared in people who had suffered a vitreous hemorrhage which caused serious loss of vision. Early vitrectomy was compared to deferred vitrectomy to find out if better vision can be achieved by operating soon after the hemorrhage has occurred or by waiting a year in the hope that the hemorrhage will clear spontaneously. Vitrectomy involves surgical removal of the blood and scar tissue from the center of the eye. The investigators found that 25 percent of eyes which underwent early vitrectomy had a visual acuity of 10/20, while only 15 percent of those in the deferred treatment group had achieved such good results. The beneficial effect of early treatment was even more apparent in patients who had beginning juvenile diabetes. The investigators concluded that early vitrectomy can improve chances of long term recovery of good vision in some eyes.

The NEI is concerned not only with appropriate management of diabetic eye disease once it develops, but also with its prevention. In one ongoing multicenter study involving 600 insulin-dependent diabetics, a new drug called sorbinil is being evaluated to determine whether it can protect the retina from diabetes-induced damage. The NEI is sponsoring the study in collaboration with Pfizer Incorporated, the pharmaceutical firm that developed the drug. During this past year, efforts to recruit patients were expanded and the number of patients enrolled increased dramatically.

Age-related macular degeneration (AMD) is the leading cause of severe visual loss among people age 60 and older. Research on the treatment of neovascular AMD, a form of the disease that poses the most serious threat to sight, is being conducted by the NEI-supported Macular Photocoagulation Study Group (MPS). Since 1982 when MPS investigators first reported that argon laser treatment for neovascular AMD is beneficial, it has become the standard treatment for this disease. Now, these investigators are evaluating the krypton laser in the treatment of some patients who cannot be helped by the argon laser.

An NEI intramural research team is also studying long-term protective measures that may someday be used to keep AMD from reaching the stage when laser treatment is necessary. Patients are asked to protect their eyes from bright light by using specially tinted eyeglasses. In addition, the investigators are evaluating antioxidant medications that may help to slow or prevent aging-related changes in the retina. Researchers hope that these simple measures will reduce the risk of visual loss from AMD.

Glaucoma is another eye disease that affects middle-aged or older people, and is a major cause of blindness. About 1.5 to 2 million Americans have the common (open-angle) form of glaucoma. The NEI is supporting a program of basic and clinical research to learn more about the mechanisms that cause increased intraocular pressure and to develop more effective means of early detection. Currently, glaucoma specialists at medical centers in Atlanta, Boston, Los Angeles, Milwaukee, New York City, Philadelphia, Columbus (Ohio), Chicago, and New Orleans are participating in an NEI-funded clinical trial to determine whether argon laser treatment may be an effective means of controlling intraocular pressure and preventing visual loss in newly diagnosed patients with open-angle glaucoma.

It is estimated that one out of every four schoolchildren in the United States has a vision problem. Finding more effective ways to diagnose, treat, and prevent the disorders that cause visual impairment in childhood is a major goal of NEI research. One of the main blinding disorders of childhood now receiving attention in the NEI research program is retinopathy in premature infants. In this disease abnormal blood vessels and fibrous tissue grow on the surface of the retina--the light-sensing tissue of the eye. Severe retinopathy in premature infants can end in detachment of the retina and permanent visual impairment. Retinopathy has been increasing in frequency in recent years because of improved survival rates among very small premature infants, who are at particular risk for this eye condition.

In the past year, the NEI has inaugurated a major clinical trial to evaluate cryotherapy as a method of halting the progression of retinopathy in severely affected infants. In this procedure an instrument called a cryoprobe, which freezes the tissue it touches, is applied to carefully selected sites on the outside of the eye. The aim is to alter the underlying retinal tissue in such a way that abnormal blood vessels and fibrous tissue will not grow there; the areas treated by cryotherapy would thus act as a barrier to prevent the spread of the abnormalities that threaten to detach the retina. It is expected that about 6000 infants of very low birthweight will be examined for signs of ROP, and 300 will be enrolled in the clinical trial using cryotherapy.

Other genetic and developmental conditions now being studied by NEI-supported investigators are: retinoblastoma (a rare ocular cancer), congenital cataract, amblyopia ("lazy eye"), retinitis pigmentosa (a blinding hereditary disease that strikes children and adolescents), and various refractive errors such as myopia (nearsightedness). This research is expected to yield advances in diagnosis, treatment, and prevention that will improve the vision health of American children and, in so doing, spare many people from the lifelong burden of visual handicaps acquired in childhood.

AIDS Research

The National Eye Institute is participating in the global attack on acquired immunodeficiency syndrome (AIDS). The request excludes $104,000 for AIDS, which are under the single AIDS appropriation in OASH. Comparable amounts for 1986 are $96,000 and for 1985 $200,000. Collaborative studies conducted at the NEI's clinical research facilities are expected to yield important information about the disease, its detection, and possible treatments.

During the past year, NEI investigators detected the virus associated with AIDS, HTLV-III, in the tears of a patient with this disease, and also in the outer layer of the conjunctiva, the transparent membrane that covers the white of the eye and the inside of the eyelids. The recovery of HTLV-III from tears and conjunctival epithelium is consistent with recent studies isolating HTLV-III in other tissues and secretions from AIDS patients, including blood, semen, saliva, brain, and bone marrow.

National Eye Institute

Retinal and Choroidal Diseases

1987 Authorization: Indefinite.

Budget Authority:

1986 Appropriation	1986 Available after sequestering	1986 Revised Estimate	1987	Increase or decrease
$77,300,000	$73,401,000	$71,228,000	$70,689,000	-$539,000

Purpose and Method of Operation

Most blindness and visual disability in this country is caused by disorders of the retina, the light-sensitive tissue that lines the back of the eye. Closely related to and helping nourish the retina is the underlying blood vessel layer--the choroid. Because of the interrelationship of the two structures, diseases affecting one usually involve the other. For most retinal and choroidal diseases, there is currently no means of cure or prevention. Increasing knowledge of the fundamental processes underlying retinal and choroidal function is therefore of primary importance to this NEI program.

Under this program, NEI supports basic and applied studies on the structure and function of the retina in health and disease. Included are studies on blood vessel abnormalities such as diabetic retinopathy, inflammatory disorders, tumors, developmental and hereditary disorders, macular degeneration, retinal detachment, environmentally-induced disorders, and the functioning of the photoreceptors. Research is funded by grants and contracts, cooperative agreements, institutional training grants, and individual fellowships.

Rationale for the Budget Request

The 1987 budget request for the Retinal and Choroidal Diseases program is $70,689,000, a decrease of $539,000 from the 1986 estimate. The 1987 request includes support for 427 research project grants, 28 core grants, 14 grants in the other research category, 85 full-time-training positions and 55 research and development contracts.

The NEI has the second largest diabetes research budget at NIH. Funding for diabetes research is emphasized because of the large number of individuals at risk of developing diabetic retinopathy and cataracts. We know that 90 percent of people with insulin dependent diabetes will have some degree of retinopathy after 15 years. Moreover, after 30 years, 50 percent will have proliferative disease. The results of a clinical trial which demonstrated the success of treating advanced diabetic retinopathy with the laser were reported a number of years ago. Currently, ongoing clinical trials have begun to show us the optimum time to use photocoagulation in the course of diabetic retinopathy and to use a surgical procedure known as vitrectomy.

Another ongoing clinical trial related to diabetes is the Branch Vein Occlusion Study. In the course of this study it has already been found that laser treatment can improve central vision in some patients who have experienced blockage of a retinal vein. This is a problem that affects many people having high blood pressure or diabetes. Exploration of the risks and benefits of lasdr treatment in people with this disorder is continuing.

Investigation of the mechanisms underlying ocular inflammatory disease is important to the ophthalmic immunologic community and to immunologists in general, since it is possible to discern immune responses in the eye which are sometimes impossible to study in other organ systems. Tools that permit a more effective evaluation of both clinically obtained specimens and laboratory models have been developed. The use of monoclonal antibody technology to better define immune cell components has been a cornerstone of these advances. This complex technique identifies, localizes, and isolates cellular components.

Recombinant DNA and monoclonal antibody technology are advancing at an explosive pace. Molecular genetics research has succeeded in isolating various human and viral genes important in malignant tumors, and the cellular roles played by these genes and their products are under intensive investigation. Studies of retinoblastoma, a malignant tumor of the eye, have revealed a new class of oncogene, i.e., one where recessive mutations predispose to malignancy. Monoclonal antibodies play a key role in demonstrating the various potential ways a retinoblastoma cell can reproduce in tissue culture, thereby elucidating the cell of origin of the tumor. Utilization of advances in basic science for the investigation of eye cancers will continue to be aggressively pursued.

Research on retinitis pigmentosa (RP) and other retinal disorders has accelerated greatly over the last few years. Cell biologists, biochemists, and neurobiologists have brought their laboratory expertise to bear on many forms of retinal degeneration in laboratory animals, patients with retinitis pigmentosa, and donor eye tissues. Through these collaborative efforts our knowlege of possible retinal degenerative mechanisms has been expanded. As mentioned earlier, the application of molecular genetic techniques has recently revealed the localization on the X-chromosome of the gene that causes one form of RP. Thus, research in this area is rapidly progressing in important directions that did not even exist only a few years ago.

Continued refinements in surgical techniques and instrumentation have led to further advances in the management of retinal detachment and vitreous hemorrhage conditions. A new clinical trial begun early this year will address the most common cause for failure of surgery for detached retina--the development of cellular proliferation and membrane contraction which prevent the retina from maintaining its normal position in the eye. This condition, proliferative vitreoretinopathy, in its most advanced form is virtually inoperable using currently available surgical techniques. New procedures have recently been developed for applying a silicone gel to keep the retina in place, at the same time blocking cellular proliferation and subsequent retinal detachment. In the Multicenter Clinical Trial of Silicone Oil in Vitreoretinopathy, NEI-supported researchers will evaluate the safety and efficacy of these silicone implants in the preservation of vision.

Retinal detachment is an important clinical problem about which more information on its causes, prevention and treatment is needed. The NEI will sponsor a workshop entitled "Cell Biology of Retinal Detachment" which will bring together basic scientists and clinicians in order to examine this problem in light of recent advances in the burgeoning field of cell biology. Results and conclusions from this workshop will be transmitted to the National Advisory Eye Council to assist in identifying research opportunities and in charting future directions for research on retinal detachment.

Impact Data	1986 Appropriation	1986 Available after sequestering	1986 Revised estimate	1987
Res. project grants				
Number	455	451	439	427
Amount	$61,402,000	$58,187,000	$56,014,000	$55,009,000
Res. centers				
Number	28	28	28	28
Amount	5,967,000	5,710,000	5,710,000	5,275,000
Other research				
Number	19	19	19	14
Amount	1,197,000	1,145,000	1,145,000	1,055,000
Training				
Number	81	81	81	82
Amount	2,085,000	1,996,000	1,996,000	2,135,000
Research and Dev. contracts				
Number	48	48	48	55
Amount	6,649,000	6,363,000	6,363,000	7,215,000
Total	77,300,000	73,401,000	71,228,000	70,689,000

National Eye Institute

Corneal Diseases

1987 Authorization: Indefinite.

Budget Authority:

1986 Appropriation	1986 Available after sequestering	1986 Revised Estimate	1987	Increase or decrease
$28,200,000	$27,188,000	$26,253,000	$26,149,000	-$104,000

Purpose and Method of Operation

This program encompasses research on diseases of the cornea--the transparent structure at the front of the eye that helps focus incoming light rays--and of the external ocular structures, including conjunctiva and lids. Because the cornea is the most exposed surface of the eye, it is particularly vulnerable to damage from injury, infection, toxic agents, and environmental pollutants.

The Corneal Diseases program of the National Eye Institute is divided into the following five subprograms: external ocular infections and inflammatory diseases, ocular surface problems, refractive problems and contact lenses, corneal edema, and corneal transplantation and wound healing. Research is funded by grants and contracts, cooperative agreements, institutional training awards, and individual fellowships.

Rationale for the Budget Request

The 1987 budget request for the Corneal Diseases program is $26,149,000, a decrease of $104,000 from the 1986 estimate. The 1987 request includes support for 178 research project grants, 5 grants in the other research category, and 43 full-time-training positions.

Herpes simplex virus (HSV) is the most common cause of infectious blindness in the United States; approximately 500,000 cases are reported annually. The propensity of this disease to become latent and then periodically and unpredictably recur makes it a difficult clinical problem for patients and ophthalmologists alike. The key to control of the disease is in improved understanding of the pathogenesis of the recurrent herpes infection. Recent developments in recombinant DNA technology have made it possible to isolate individual genes from the HSV chromosome and study how they are regulated during virus replication. In addition, genes for the major viral antigens expressed on the surface of corneal cells during ocular herpes infection have been cloned. These developments in the molecular biology of HSV have opened up new opportunities for investigating the pathogenesis and latency of HSV at a molecular level and for creating new vaccines for lifelong protection against HSV infection.

A new drug, vidarabine, whose effectiveness in the treatment of herpes virus infection of the cornea has been tested under grants from the NEI, is now available as a prescription ophthalmic ointment. Vidarabine is expected to be especially valuable in treating patients who do not respond to idoxuridine, the only other drug useful in treating herpes virus infections of the eye, or who experience undesirable side effects with that drug.

Ocular surface disorders continue to be an important area of research because of their relative frequency and severity. These disorders involve the tear film, the conjunctiva, and the cornea and cause redness, discharge, pain, and reduced vision. In some cases the abnormalities lead to ulceration and scarring of both the cornea and conjunctiva, resulting in the need for corneal transplantation from a donor or in permanent disability.

Over the past three years, considerable attention has been focused on the tear film and its role in maintaining the health of ocular surface cells. A recent Tear Film Symposium sponsored by the NEI at Texas Tech University, brought together researchers from the U.S. and abroad to discuss the current status of tear film research and therapy. The outcome of these deliberations was encouragement for further research to increase understanding of tear film composition and function.

Corneal transplantation has the highest success rate of all tissue transplant operations and has resulted in the restoration of sight to hundreds of thousands of persons. However, between 20 and 50 percent of corneal grafts are rejected, depending on the particular condition for which the procedure was done. To improve the success rate of corneal transplantation, the immune rejection phenomenon must be better understood. Investigators are finding that corneal grafts that have been soaked in a solution containing antibody against the human lymphocyte antigens (HLA) found on the surfaces of most tissues have an increased survival time when compared to unsoaked grafts.

The immunologic basis for this protection of corneal grafts by soaking in antibody solution and the biological characteristics of the antigens on the surface of the cornea are currently being studied. The effect of HLA matching of donor corneas with recipient tissue on the outcome of the graft is being evaluated in a multi-center clinical trial.

The ocular surface's seeming increased vulnerability to injury when there is nutritional vitamin A deficiency is being investigated. Vitamin A deficient rabbits with surface lesions similar to those found in children who are vitamin A deficient are being studied. In addition, clinical studies of abnormalities of the ocular surface in vitamin A deficient children in developing nations are now underway to define the mechanism responsible for the high incidence of blindness associated with measles and other infections.

In addition to research which has contributed to the development, testing, and subsequent FDA approval of new extended-wear and gas-permeable contact lenses, much effort has been dedicated to the study of effects of contact lenses on the cornea and surrounding tissues. Related to this, new clinical instrumentation for monitoring corneal and visual changes has been developed. This includes: photoelectric keratoscopes for measuring corneal contour, computer-assisted analysis of corneal topography, the electronic digital pachymeter for monitoring corneal thickness, and the specular microscope for observing living corneal cells in the intact human eye. Another new instrument, the fluorophotometer, has been used to study the flow of tears under contact lenses and to examine tear secretion, tear flow rates, and their effect on the cornea.

Impact Data	1986 Appropriation	1986 Available after sequestering	1986 Revised estimate	1987
Res. project grants				
Number	184	185	180	178
Amount	$26,728,000	$25,779,000	$24,844,000	$24,853,000
Other research				
Number	9	9	9	5
Amount	304,000	291,000	291,000	176,000
Training				
Number	52	52	52	43
Amount	1,168,000	1,118,000	1,118,000	1,120,000
Total	28,200,000	27,188,000	26,253,000	26,149,000

National Eye Institute

Cataract

1987 Authorization: Indefinite.

Budget Authority:

1986 Appropriation	1986 Available after sequestering	1986 Revised Estimate	1987	Increase or decrease
$14,254,000	$13,792,000	$13,311,000	$13,275,000	-$36,000

Purpose and Method of Operation

A cataract is a cloudy or opaque area in the eye's lens that can develop over a period of years or within just a few months. If the lens becomes clouded with a cataract, the passage of light is obstructed and vision may be impaired. A cataract results from complex changes in the chemical composition of the lens, which scientists only partially understand.

NEI's Cataract Program supports studies on how and why cataracts develop, ways to prevent cataracts or slow their progress, the safety and effectiveness of new surgical and other techniques for treating cataracts, and better methods to correct vision after cataract surgery. Research in this program is funded through research grants and contracts, cooperative agreements, institutional training awards, and individual fellowships.

Rationale for the Budget Request

The 1987 budget request for the Cataract program is $13,275,000, a decrease of $36,000 from the 1986 estimate. The 1987 request includes support for 120 research project grants, 1 core grant, 3 grants in the other research category, and 3 full-time-training positions.

About 60 percent of people between the ages of 65 and 74 show some signs of opaque areas in the lenses of their eyes. About 3.3 million people in the United States have some degree of visual impairment from cataracts and at least 43,000 people are actually blind from this disorder--making it the third leading cause of legal blindness in this country. Each year approximately 4,700 new cases of blindness resulting from cataracts occur. This number will increase, and its significance will become greater, as the ratio of older people in the U.S. population increases.

At present, surgery to remove the opaque lens is the only effective way of treating cataracts. Techniques developed over the past 25 years have made cataract extraction one of the safest and most successful of all major operations. Nonetheless, because it is always desirable to avoid surgery if possible and because complications still occur following cataract extraction in a small percentage of cases, the NEI devotes most of its funding in the Cataract program to discovering the means for preventing or slowing the development of cataracts or of treating them nonsurgically. The emphasis is on investigating the mechanisms of lens transparency or opacification, and on clinical and epidemiological research into patterns of cataract formation in humans.

Progress has been made in understanding the normal lens. As a result of a major scientific effort over the past few years to identify the cell biology, molecular biology, and biophysical properties of the lens, new knowledge concerning embryologic lens induction and differentiation has been gained, including an assessment of some of the factors involved in cell elongation and epithelial cell and fiber cell differentiation in vivo and in culture. Numerous experiments have indicated the importance of hormones and growth factors in the control of cell division in the lens epithelium.

Significant advances have been made in characterizing crystalline lens structures, and molecular studies on crystalline lens genes have been initiated. Crystallins are the lens proteins responsible for transparency. The cloning of crystallin genes in bacteria holds promise for further elucidation of protein and genetic activity in the lens.

Anatomical techniques such as scanning and transmission electron microscopy and freeze fracturing have yielded a better view of the morphology of lens fibers. Considerable progress has been made in understanding the chemistry and morphology of the lens cytoskeleton. Transport studies have delineated the processes involved in maintaining the metabolic and nutritional integrity of the lens. Extensive research has continued in lipid and carbohydrate metabolism, and a more unified view of lens metabolism is emerging.

Researchers studying lens chemistry are investigating why lens protein may lose its natural biochemical structure during the aging process, when a head injury occurs, or by such diseases as diabetes. It appears that a cataract forms when lens cell proteins clump together into huge molecules. As incoming light hits these molecules, it scatters and decreases lens transparency. To perform these studies NEI-supported investigators are employing nuclear magnetic resonance (NMR), a noninvasive technique to analyze the chemical activity in a living lens tissue without harming or even touching it. The NMR equipment generates a powerful but harmless magnetic field around the lens, revealing its living chemical makeup. The research team has used NMR to elucidate the chemical pathway taken inside the lens during the formation of one kind of cataract called the "sugar cataract". NMR experiments offer the possibility of detecting changes in lens biology well before the appearance of an opacity.

During the past year, the NEI initiated the "Case Control Study of Senile Cataract". This study, being conducted in Boston, will involve 1,500 patients. Senile or aging-related cataract is a major cause of blindness and visual disability throughout the world. Despite its high frequency and public health impact, the factors predisposing to senile cataract development are largely unknown. The aim of this study is to evaluate associations of risk factors such as nutritional status and family history with major types of senile cataract and to evaluate methods of cataract classification. By accomplishing these objectives, the study has the potential of contributing to our understanding of what causes cataracts and eventually to how they may be prevented.

Impact Data	1986 Appropriation	1986 Available after sequestering	1986 Revised estimate	1987
Res. project grants				
Number	117	118	115	120
Amount	$13,870,000	$13,424,000	$12,943,000	$12,967,000
Res. centers				
Number	1	1	1	1
Amount	133,000	128,000	128,000	125,000
Other research				
Number	4	4	4	3
Amount	156,000	149,000	149,000	109,000
Training				
Number	4	4	4	3
Amount	95,000	91,000	91,000	74,000
Total	14,254,000	13,792,000	13,311,000	13,275,000

National Eye Institute

Glaucoma

1987 Authorization: Indefinite.

Budget Authority:

1986 Appropriation	1986 Available after sequestering	1986 Revised Estimate	1987	Increase or decrease
$15,830,000	$15,300,000	$14,731,000	$14,684,000	-$47,000

Purpose and Method of Operation

Glaucoma usually occurs when the out flow of aqueous humor, a fluid constantly produced in the eye is impaired leading to an excessive level of pressure within the eye. The building of pressure gradually destroys the optic nerve, which carries visual messages to the brain and allows sight. This damage is irreversible.

The Glaucoma Program promotes research on preventing blindness from glaucoma through studies of the optic nerve, improving methods of lowering intraocular pressure, developing methods for very early detection and treatment of glaucoma, and predicting its clinical course. These objectives are accomplished through research project grants and contracts, cooperative agreements, individual fellowships, and institutional training awards.

Rationale for the Budget Request.

The 1987 budget request for the Glaucoma program is $14,684,000, a decrease of $47,000 from the 1986 estimate. The 1987 request includes support for 103 research project grants, 2 grants in the other research category, and 2 full-time-training positions.

Glaucoma is one of the leading causes of visual impairment in the United States and may be the major cause of blindness among black Americans. It is estimated that, 62,000 people were blind from glaucoma in this country in 1978. A total of 1.5 to 2 million people actually have the disease but, fortunately, most of them will be able to avoid serious visual impairment through adequate medical care. The most common form of the disease, primary open-angle glaucoma, is associated with aging and affects about three percent of people aged 70 years and older.

Epidemiologic studies are underway to determine the risk factors for open-angle glaucoma, especially to evaluate possible racial differences in these factors. In population studies, blood pressure and body weight have been found to be positively correlated with intraocular pressure. Myopia has been demonstrated to be a risk factor for open-angle glaucoma. Epidemiologic evidence suggests that migraine is also a risk factor. A better understanding of the risk factors for glaucoma developed through the use of modern epidemiologic methods, could well improve the clinician's prognostic ability, shed light on disease mechanisms, and perhaps point the way to earlier and better treatments.

A number of clinical studies are evaluating aspects of medical therapy for glaucoma. Preliminary studies indicate that some patients who seem to be losing vision from glaucoma with apparently normal levels of intraocular pressure have, in fact, sporadic elevations of pressure that are not being detected during office visits. To remedy this, a self-tonometer has been developed for home monitoring of intraocular pressure.

A special eyedrop dispenser, that externally resembles an ordinary bottle but internally contains a computer which records times of eyedrop administration, is being used to monitor patient compliance with medical treatment of glaucoma. This particular device is important because studies indicate that few patients comply well with instructions for their glaucoma medications.

Two therapeutic randomized clinical trials also are underway. In one, 5-fluorouracil, a chemical that inhibits cell proliferation, is administered postoperatively under the conjunctiva of the eye. Administration of this chemical has been shown to enhance the success of filtration surgery in high risk patients. The purpose of this trial is to define further the safety and efficacy of this treatment. Numerous previous studies supported by the Glaucoma Program have documented the efficacy, relative safety, and potential risks of argon laser trabeculoplasty, a procedure that increases outflow of aqueous humor. Now the Glaucoma Laser Trial is comparing the efficacy of this therapy with that of traditional medical treatment with topical drugs in the newly diagnosed patient with primary open-angle glaucoma.

Understanding the physiology of aqueous humor formation has increased through the development of aqueous fluorophotometry, a method for measuring aqueous humor flow. Several investigators are applying this technique to studies in the eyes of rabbits, monkeys, and humans. Fluorophotometry has already provided important information about the physiologic mechanisms of drug actions, particularly in humans, basic physiological data on the diurnal rhythm of aqueous humor formation, and information on changes in aqueous formation during disease states.

Significant optic nerve injury precedes and accompanies the initial recognition of visual field loss in glaucoma. Understanding the mechanisms by which the optic nerve is injured in glaucoma is being increased by new methods for detecting early nerve damage. Nerve fiber layer photography has been improved and demonstrated to be a clinically useful method of detecting early optic nerve injury. Future experiments with this technique will determine its use as a predictor of which eyes with ocular hypertension are likely to develop visual field defects.

Because intraocular pressure cannot be manipulated experimentally and the optic nerve cannot be observed directly in man, it is especially important to study in appropriate animal models the effects on the optic nerve of the range of pressures encountered in glaucoma. In this regard, monkey studies are extremely useful for investigating optic nerve injury in glaucoma, because the optic nerve anatomy in the monkey and its pattern of injury are so similar to those in man. Studies of the physiology of the optic vascular system under conditions of elevated intraocular pressure in this model suggest that the primary source of injury in glaucoma is mechanical rather than vascular. These studies add to our understanding of the mechanisms of optic nerve injury.

Impact Data	1986 Appropriation	1986 Available after sequestering	1986 Revised estimate	1987
Res. project grants				
Number	107	108	107	103
Amount	$15,672,000	$15,148,000	$14,579,000	$14,588,000
Other research				
Number	5	5	5	2
Amount	113,000	108,000	108,000	47,000
Training				
Number	2	2	2	2
Amount	45,000	44,000	44,000	49,000
Total	15,830,000	15,300,000	14,731,000	14,684,000

National Eye Institute

Strabismus, Amblyopia, and Visual Processing

1987 Authorization: Indefinite.

Budget Authority:

1986 Appropriation	1986 Available after sequestering	1986 Revised Estimate	1987	Increase or decrease
$34,189,000	$32,796,000	$31,730,000	$31,631,000	-$99,000

Purpose and Method of Operation

The Strabismus, Amblyopia, and Visual Processing program promotes and supports research on the structure, function, and development of the ocular muscles and those portions of the brain that make vision possible. This research is directed toward gaining a better understanding of normal vision and of the causes of visual deficits and blindness that do not appear to result from specific dysfunction of the eye itself. This program is funded through research grants and contracts, cooperative agreements, institutional training awards, and individual fellowships.

Rationale for the Budget Request

The 1987 budget request for the Strabismus, Amblyopia and Visual Processing program is $31,631,000, a decrease of $99,000 from the 1986 estimate. The 1987 request includes support for 275 research project grants, 8 grants in the other research category, and 60 full-time-training positions.

Seeing involves a series of highly complex processes. These processes include searching and scanning eye movements to localize the image on the retina, vergence and accommodation to refine the localization and to achieve focus, and visual processing, so that objects are actually seen in detail, depth, and color. A disturbance to any part of this elaborate and precise system can lead to serious visual disorders, such as amblyopia (severely reduced vision in one eye), strabismus (misalignment of the eyes or "cross-eye"), nystagmus (irregular eye movements), and myopia (nearsightedness).

These conditions collectively affect over 10 percent of our population. Although seldom causing legal blindness, they produce considerable visual impairment and disability, interfere with learning and working, and may even cause psychological problems because of their effect on appearance.

Further advances in clinical investigations of normal and abnormal visual processing depends upon expanding our knowledge of basic visual mechanisms at the cellular level. Factors that stimulate, regulate, or guide neural growth in the visual system are the focus of active research efforts. Studies of normal development in the animal embryo and during the postnatal period have provided new insights on how and why neural growth occurs, both normally or abnormally.

Thanks to recent innovative developments in molecular research techniques, investigators can now manipulate the intracellular environment. Using these methods they can label neurons in the central visual pathway of normal and visually deprived animals to describe the effects of visual deprivation at the cellular level. The realization that, at least in lower vertebrates, neural connections can be broken and formed by different manipulations has led to new ideas on the conditions required for the stable transmission of impulses in the visual pathway. This recent work has expanded our understanding of the cellular basis of blindness caused by strabismus and other forms of visual deprivation in children.

Studies of animal models of visual development and abnormal visual experience have contributed immensely to the clinician's knowledge and understanding of the conditions seen in patients. By introducing the concept of the "critical period" of visual development, clinicians have been made more conscious of the importance of early diagnosis and treatment in their patients and of the need to study early visual development in infants. Recent clinical studies have centered on visual acuity and resolution and color perception in human infants.

In studies of color vision in infants, preferential looking (PL) experiments have shown that newborns can discriminate between colored and grey objects. Using PL it has also been demonstrated that two separate receptor types and chromatic pathways are functioning by the fifth week of postnatal life, and that the development of the blue-yellow pathways lags behind that of the red-green. The efforts by investigators to extend their laboratory observations with clinical PL types of experiments are important. Research such as this will help bring clinicians closer to the goal of being able to quantify visual acuity and other functions in infants and toddlers. This would allow for earlier diagnosis of possible disorders and prompt intervention with available therapies.

A childhood eye disorder of major importance in this research program is strabismus. In this very common condition, an imbalance of the eye muscles causes one or both eyes to turn inward (cross-eye) or outward (wall eye). Each year more than 80,000 people undergo eye muscle surgery for correction of this disorder. One of the major problems confronting the surgeon is determining how much correction is required to bring the patient's eyes into alignment. Because it is difficult for doctors to gauge this precisely, many children with surgically correctable strabismus have to undergo several operations before alignment is achieved.

To improve presurgical assessment of children with one common form of strabismus, the NEI is supporting a multicenter clinical trial that will determine whether children slated for strabismus surgery are more likely to have a successful outcome if the doctor first performs a prism adaptation test. In this procedure, the child is fitted with a succession of very strong glasses. These contain prisms that bend light in such a way as to encourage the misaligned eye to turn in the proper direction. By determining how strong the prisms must be to achieve this temporary alignment, the doctor obtains an estimate of the amount of surgical correction required to achieve permanent alignment. If estimates obtained in this way prove to be a useful guide for surgeons, the method may greatly reduce the number of repeat operations required for correction of strabismus.

A significant number of Americans have what is called "low vision". Although most are nearly blind, more than 90 percent retain a degree of usable residual vision in spite of their impairment. In its most recent assessment of needs and opportunities in vision research, the National Advisory Eye Council addressed the need for techniques that are related to determining the low vision patient's ability to function effectively in his environment. In response to this need, the NEI, has expanded its program of research on assessing functional vision in people with low vision. This research will pursue the relationship between information derived from laboratory tests of visual function and the patients' ability to perform common visually based tasks in their everyday lives. The goal is to develop a battery of tests that could be used by eye care specialists to generate a visual function profile for each of their patients and then predict how their functioning will improve with the use of specific visual aids.

Impact Data	1986 Appropriation	1986 Available after sequestering	1986 Revised estimate	1987
Res. project grants				
Number	278	279	273	275
Amount	$31,743,000	$30,456,000	$29,390,000	$29,844,000
Other research				
Number	13	13	13	8
Amount	608,000	582,000	582,000	389,000
Training				
Number	69	69	69	60
Amount	1,838,000	1,758,000	1,758,000	1,398,000
Total	34,189,000	32,796,000	31,730,000	31,631,000

National Eye Institute

Vision Research Facilities

1987 Authorization: Indefinite.

Budget Authority:

1986 Appropriation	1986 Available after sequestering	1986 Revised Estimate	1987	Increase or decrease
$3,300,000	$3,158,000	$3,158,000	--	$-3,158,000

Purpose and Method of Operation

The National Eye Institute administers a Vision Research Facilities Grant Program under the authority of the Public Health Service Act. Under this legislation the NEI has received funds to expand the capacity for basic, applied, and clinical research for public and nonprofit private vision research facilities through new construction, alteration and renovation of existing structures, and acquisition of high technology equipment and instruments.

Rationale for the Budget Request

Funds from this program were reallocated to areas of higher priority in 1987. Therefore, the request does not provide support for the NEI vision research facilities program.

Today's scientific investigation requires technically advanced facilities and instrumentation. The aim of NEI's construction authority has been the renewal and continuing maintenance of an adequate base for the nation's vision research effort. In fiscal year 1985 the NEI awarded six grants for new construction, three for alterations and renovations to existing space, and 11 grants for the acquisition of high technology equipment. This program is assisting universities actually engaged in vision research to keep pace with the latest advances in biomedicine and to update their outmoded facilities to meet changing health and safety codes.

National Eye Institute

Intramural Research

1987 Authorization: Indefinite.

Budget Authority:

1986 Appropriation	1986 Available after sequestering	1986 Revised Estimate	1987	Increase or decrease
$16,051,000	$15,360,000	$15,360,000	$16,723,000	$1,363,000
		(FTEs: 140)	(140)	(--)

Purpose and Method of Operation

The Intramural Laboratory and Clinical Research program of the National Eye Institute is divided into seven components: the Clinical Branch, the Laboratory of Sensorimotor Research, the Laboratory of Molecular and Developmental Biology, the Laboratory of Ophthalmic Pathology, the Laboratory of Immunology, the Laboratory of Retinal Cell and Molecular Biology, and the Laboratory of Mechanisms of Ocular Diseases. In fiscal year 1986 the Intramural Research Program was reorganized to promote research on the latest investigational techniques available in immunology, cellular and molecular biology, and in deciphering the mechanisms of ocular disease. The Intramural Program also includes the Biometry and Epidemiology Program which plans, develops, and carries out population and other epidemiological studies on the causation, prevention, and treatment of vision disorders.

Rationale for the Budget Request

The 1987 budget request for Intramural research is $16,723,000 an increase of $1,363,000 over the 1986 estimate. The increase will provide for current services and allow for further exploitation of new and complex research techniques applied in particular and basic studies of eye diseases.

The NEI intramural program is built upon a strong base of multidisciplinary research activity. It is focused on areas of research not extensively covered in the extramural vision research community, such as epidemiology and epidemiologic approaches to clinical research, immunology, combined laboratory and clinical approaches to neuro-ophthalmic problems, applications of basic clinical psychophysics, and most recently, molecular biology.

The use of genetic engineering or recombinant DNA technology has greatly accelerated the pace of eye research. This new research method may ultimately yield a detailed understanding of the molecular basis for the development, functional organization, and expression and regulation of genetic information in the eye and visual system. Moreover, current studies are bringing us closer to the time when it will be possible to prevent or correct genetic defects that cause hereditary eye disease. Much of the pioneering work in this field is being done within NEI's intramural program.

Numerous gene families produce important proteins in the eye. Recombinant DNA techniques are being used to study three such families, namely the crystallins (lens proteins responsible for transparency), collagens (extracellular proteins controlling the shape and structure of the eye), and the opsins (retinal proteins responsible for transforming light into nerve impulses). Such work has relevance for understanding the molecular basis for cataract, genetic diseases, defects related to the ocular aspects of diabetes, and color vision defects.

In the past year, there was a major breakthrough using molecular biological techniques in basic retinal studies. NEI investigators succeeded in isolating and cloning the gene that codes for a little-understood protein that helps to regulate the movement of nutrients such as vitamin A to and from the light-sensing cells of the retina. The protein is normally present in the space between these cells. Other recent work by this same team has suggested that disappearance of this protein may be one of the earliest changes detectable in some eyes with retinitis pigmentosa, a group of blinding genetic eye diseases. Thus, there is hope that further study of the protein, and the gene that codes for it, may yield valuable insights into the mechanisms underlying this group of diseases.

Even more rapid progress is occurring in the study of gyrate atrophy, another blinding disorder that is related to retinitis pigmentosa. Gyrate atrophy is perhaps the best defined of the hereditary retinal degenerations because research by NEI scientists has revealed that patients with the disease have a genetically determined deficiency in the enzyme ornithine aminotransferace (OAT). Within the past year, intramural investigators have isolated and cloned the gene for this enzyme. They are now engaged in an intensive study of the OAT gene with the hope of identifying the abnormalities that are responsible for gyrate atrophy. A long-term goal of this work is to devise a gene therapy for the disease.

Progress is being made by NEI scientists in increasing our understanding of the mechanisms by which diabetes damages tissues in the eye and elsewhere in the body. These investigators have developed a class of drugs called aldose reductase inhibitors which seem to have great potential for preventing diabetes-associated tissue damage. Aldose reductase is an enzyme that is believed to contribute to eye and nerve damage in people with diabetes.

Retinal complications of diabetes that are strongly linked to aldose reductase activity can now be reproduced in animal models. A special dog model is providing NEI investigators with an effective animal model of diabetic retinopathy that will permit adequate testing of the dosage and preventive value of new drugs that inhibit the activity of aldose reductase. It is hoped that the use of the latest and most potent inhibitors of aldose reductase in experiments with galactosemic animal models of diabetes will result in an effective treatment for diabetes that is independent of insulin and serum sugar levels.

NEI scientists are in the forefront of research on the elements of photoreception. Study of normal photoreceptor functioning is not only important in itself, but is a model for several other systems of signal transduction. Outer segments of the retinal photoreceptor cell are specialized organs designed to accept a photic stimulation, convert it into an electrophysiological response, and begin processing the signal into a visual image. Regulation within the photoreceptor cell involves multiple steps. Problems with any aspect of this process can lead to visual impairment and blindness. Through research, it has become clear that abnormal concentrations of proteins necessary to the visual cycle are involved in specific disease processes, including inherited retinal degeneration and uveitis.

In the area of clinical research, NEI scientists are tackling problems whose solutions have broad implications for biomedicine. One example is a new study of fibronectin in corneal epithelial defects. Fibronectin is a fibrous protein substance believed to be manufactured by the liver. It literally sets up a kind of scaffold for wound healing. It is part of the initial clot, attracting healing cells and providing something for them to adhere to. For the last several years an NEI researcher has explored fibronectin and its possible role in the healing of corneal wounds. The fibronectin has been isolated and put into eyedrop form for people who have suffered a traumatic injury to the eye, a chemical burn, herpes simplex infection, or dry eyes associated with rheumatoid arthritis. The initial experiments have been positive and patients are now being recruited for further evaluation of the efficacy of fibronectin drops in treating corneal epithelial defects.

The primary mission of the Biometry and Epidemiology Program (BEP) is to plan, develop, and carry out human population studies concerned with the causation, prevention, and treatment of eye diseases and vision disorders. This includes studies of incidence and prevalence of disease in defined populations, prospective and retrospective studies of risk factors, natural history studies, clinical trials, genetic studies, and studies to evaluate diagnostic procedures. The BEP also carries out a program of education in biometric and epidemiologic principles and methods for the vision research community and provides biometric and epidemiologic assistance to the NEI scientific staff.

The following two projects illustrate how the work of statisticians and epidemiologists becomes relevant to clinical colleagues. Such investigators have, for example, identified risk factors for diabetic retinopathy--factors which may predict which persons with diabetes will develop eye impairment. These were reported at a recent Symposium on Eye Disease Epidemiology sponsored by the BEP staff. Their study revealed that poor control of blood sugar levels may well be a contributing factor to the high prevalence of diabetic retinopathy in the population analyzed.

Another BEP project, the Eye Disease Case Control Study, is being conducted at four clinics in Milwaukee, Chicago, Boston, and New York City. The objective of this study is to isolate causative or risk factors for the development of several eye diseases. Individuals who have recently been identified as having certain eye diseases will be given thorough ocular and physical examinations and the result will be compared to those of control subjects who have also been examined. The diseases to be studied include retinal artery and vein occlusion, age-related maculopathy, a form of retinal detachment, and uveitis.

National Eye Institute

Research Management and Support

1987 Authorization: Indefinite.

Budget Authority:

1986 Appropriation	1986 Available after sequestering	1986 Revised Estimate	1987	Increase or decrease
$5,948,000	$5,591,000	$5,591,000	$6,050,000	$459,000
		(FTEs: 63)	(63)	(—)

Purpose and Method of Operation

This budget activity provides salaries and other expenses for the Institute's two major administrative components. The Office of the Director is the focal point for decision-making regarding the overall scientific and administrative direction of Institute programs. This staff includes the Office of Program Planning, Analysis, and Evaluation; the Office of Scientific Reporting; the Office of Financial Management; the Office of Personnel Management; the Office of General Administration; and the coordination of international activities and liaison with international agencies. The following are responsible for awarding and managing NEI research grants, training grants, and research and development contracts: the Office of Associate Director for Extramural and Collaborative Programs and supporting staff including the Extramural Services Branch; the Retinal and Choroidal Diseases Branch; the Strabismus, Amblyopia, and Visual Processing Branch; and the Anterior Segment Disorders Branch.

Rationale for the Budget Request

The 1987 budget request for Research Management and Support is $6,050,000, an increase of $459,000 over the 1986 estimate. This level provides funds for increased mandatory costs and will make it possible to upgrade the Institute's management information systems.

The Office of Program Planning, Analysis, and Evaluation is responsible for all NEI program planning, analysis, and evaluation activities--including the development and maintenance of a computerized management information system--and for legislative and other program coordinating activities. The planning staff has among other accomplishments developed a fluid, workable, and practical system for detailed, comprehensive program planning that is both highly useful to the Institute and well-regarded by the scientific community upon which NEI largely depends for accomplishing its mission.

During FY 1985, this Office prepared a draft of the detailed Midcourse Evaluation of all NEI programs, subprograms, and research areas contained in the National Advisory Eye Council's comprehensive five-year National Plan, Vision Research--A National Plan: 1983-1987. The staff also further developed, refined, and updated the system for tracking applications and funded projects--both in terms of their relevance to the recommendations of the recent National Plan and to the new priorities that have been developed by the ongoing Midcourse Evaluation.

The Office of Scientific Reporting (OSR) provides media relations, public education, and scientific reporting services in support of the Institute's Intramural and Extramural Research Programs.

During Fiscal Years 1986 and 1987, a major objective of the OSR will be to communicate new, potentially sight-saving research results from an NEI supported clinical trial, the Early Treatment Diabetic Retinopathy Study (ETDRS) which was described earlier. Coupled with findings from a previous study, which showed that laser treatment is beneficial in more advanced stages of the disease, the recent results provide a compelling reason why people with diabetes should have regular eye examinations to determine if treatment is needed to prevent vision loss. OSR staff will disseminate the results to the biomedical community and to the general public in a broad multi-media campaign.

Another important objective during this period will be to expand OSR efforts to assist NEI intramural scientists and clinicians. The Office will develop and carry out a program aimed at increasing patient recruitment for several Clinical Branch studies. The outcome of these clinical trials may well result in improved management of people with sight-threatening diseases, such as aging related macular degeneration, and diabetes.

The objectives of the Extramural and Collaborative Program are to maintain the cooperative and collaborative relationships already established with the vision research community, expand efforts to identify and address more effectively research opportunities and needs, and meet the many and varied scientific and administrative requirements of the vision research community.

National Eye Institute
DETAIL OF PERMANENT POSITIONS

	1985 actual	1986 estimate	1987 estimate
ES-5	1	1	1
ES-4	6	6	6
ES-3	3	3	3
Subtotal	10	10	10
GS/GM-15	12	11	11
GS/GM-14	16	17	17
GS/GM-13	21	22	22
GS-12	17	17	17
GS-11	15	15	16
GS-09	13	12	12
GS-08	4	4	3
GS-07	22	21	21
GS-06	20	18	19
GS-05	13	14	12
GS-04	3	3	3
GS-03	2	4	5
GS-02	1	1	1
Subtotal	159	159	159
Grades established by act of July 1, 1944 (42 U.S.C. 207):			
Full grade	6	6	6
Subtotal	6	6	6
Ungraded	12	12	12
Total, permanent positions	187	187	187

MONDAY, MARCH 17, 1986.

NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES

WITNESSES

DR. RUTH L. KIRSCHSTEIN, DIRECTOR

DR. JAMES B. WYNGAARDEN, DIRECTOR, NATIONAL INSTITUTES OF HEALTH

DR. LEO H. VON EULER, DEPUTY DIRECTOR, NIGMS

DR. ELKE JORDAN, ASSOCIATE DIRECTOR FOR PROGRAM ACTIVITIES, NIGMS

WILLIAM T. FITZSIMMONS, EXECUTIVE OFFICER, NIGMS

NANCY VESS, DEPUTY BUDGET OFFICER, NIGMS

DENNIS P. WILLIAMS, ACTING DEPUTY ASSISTANT SECRETARY, BUDGET, DEPARTMENT OF HEALTH AND HUMAN SERVICES

Mr. NATCHER. At this time, we take up the budget request for the National Institute of General Medical Sciences, and we have before the committee Dr. Ruth L. Kirschstein, the Director.

Dr. Kirschstein, it is a pleasure to have you back before the committee. Before you give us your statement, if you would please, tell us who you have with you at the table there.

Dr. KIRSCHSTEIN. Thank you, Mr. Natcher.

To my right is Mr. Dennis Williams from the Department of Health and Human Services; Dr. James Wyngaarden, the Director of NIH; and Dr. Leo von Euler, the Deputy Director of the NIGMS; and to my left, the NIGMS Executive Officer, Mr. William Fitzsimmons; and next to him, Ms. Nancy Vess, the NIGMS Deputy Budget Officer; and Dr. Elke Jordan, the Institute's Associate Director for Program Activities.

Mr. NATCHER. We are delighted to have all of you before the committee again, and you may proceed.

OPENING STATEMENT

Dr. KIRSCHSTEIN. Mr. Chairman, I am pleased to be here again. I shall submit my statement for the record, but I would just like to emphasize certain points.

The programs of the National Institute of General Medical Sciences support basic untargeted biomedical research endeavors which continue to provide the knowledge through which specific diseases can be conquered.

The time it takes to develop basic concepts and to translate the knowledge so generated into leads regarding those many diseases not yet understood has been telescoped from years to often only months.

The fundamental biomedical research and research training efforts supported by the National Institute of General Medical Sciences are truly an investment in the future.

Mr. Chairman, I am delighted to be able to report, as did The New York Times yesterday, that two NIGMS grantees were among the 26 scientists awarded the National Science Medal by the President last Wednesday. They are Drs. Joan Steitz and George Palade of Yale University. Dr. Palade is a long-time friend of the members of this committee.

Nowhere is this natural flow of research endeavors from fundamental undifferentiated studies to disease-targeted activities better illustrated than by an account of the work of Drs. Michael Brown and Joseph Goldstein, this year's winners of both the Nobel Prize in Physiology or Medicine and the Lasker Award for basic medical research.

Their fundamental studies of steroids and lipoproteins as building blocks for cell membranes were supported by the NIGMS for a number of years. Gradually, these collaborative studies focused on a particular steroid chemical, cholesterol, and they discovered a mechanism that controls its metabolism inside the cell.

Since such basic studies of cholesterol are critical to an understanding of, and the development of preventive and treatment regimens for, atherosclerosis and other cardiovascular diseases, their research, originally supported by NIGMS, has been supported by the National Heart, Lung, and Blood Institute in recent years.

Over the past week, my colleagues have all told you about the research accomplishments occurring in their programs. For example, late last week Dr. Fauci gave you the latest information about AIDS.

The basic studies supported by NIGMS in years past in its genetics and cellular and molecular biology programs have provided fundamental knowledge regarding viral nucleic acids and how they replicate, about how molecules or viruses attach to the cell surface membranes and enter a cell, and about how a virus uses the cell's machinery to reproduce itself while destroying the cell, in the case of AIDS, destroying the T lymphocyte, one of the cells responsible for immune responses.

This research supported by NIGMS has permitted scientists studying AIDS to come to an understanding of the disease, as Dr. Fauci told you, and to know so much about the AIDS virus.

Recombinant DNA technology is enabling the development of the vaccines for AIDS. Furthermore, the fundamental studies supported by NIGMS related to the mechanism of action of drugs have greatly speeded the development of specific drugs for this dread disease.

Now, NIGMS is supporting work on new advances, the development of new, sophisticated research technologies, such as the rapid determination of DNA sequences, the isolation of very large DNA fragments, two-dimensional NMR, and more sophisticated X-ray crystallography.

There has been a dramatic expansion of the use of all these tools, as well as scientific disciplines such as chemistry. A recent National Academy of Sciences report says that chemistry will be the most important contributor to the solution of contemporary biomedical problems over the next 10 years. NIGMS provides the major support for research in chemistry at NIH.

All of these research advances, about which you have heard over the past week, have as their origins the untargeted, creative ideas of highly skilled, highly trained basic scientists.

The NIGMS, we are proud to say, has had a very large role in preparing such scientists through its research training programs. These programs have contributed about one-half of their graduates to the pool of researchers now supported by the categorical Institutes of NIH, researchers who are responsible for the advances my colleagues have outlined for you.

Thus, the programs of the NIGMS are aimed at providing the research manpower to keep up the momentum and at advancing knowledge of the fundamental cellular, molecular, chemical, pharmacologic and genetic processes so essential to developing better ways to understand, prevent and treat disease. But we must remember that there is so much yet to learn.

Mr. Chairman, the 1987 budget request for this Institute is $471,553,000. I shall be pleased to answer any questions.

[The statement of Dr. Kirschstein follows:]

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Statement of the Director
National Institute of General Medical Sciences

I am pleased to be here once again to present the programs of the National Institute of General Medical Sciences. These programs which support basic, untargeted biomedical research endeavors will continue to provide the knowledge through which specific diseases can be conquered. This ability to develop basic concepts and to rapidly translate the knowledge so generated into leads regarding those many diseases not yet understood has been telescoped from years to often only months. Yet, as each question is answered, new ones arise. What is clear is that progress builds on progress, and the future holds great promise for continuing advances. It is toward this future that the fundamental biomedical research and research training efforts supported by the National Institute of General Medical Sciences are aimed.

Nowhere is this natural flow of research endeavors from fundamental undifferentiated studies to disease-targeted activities better illustrated than by an account of the work of Drs. Michael Brown and Joseph Goldstein, this year's winners of both the Nobel Prize in Physiology or Medicine and the Lasker Award for basic medical research. Indeed, the story of the careers of Drs. Brown and Goldstein clearly demonstrates the vital role of NIH in biomedical research. Both men began their research careers in the intramural program of NIH. They then went to the University of Texas Health Science Center in Dallas, where their basic studies of cellular steroid receptors were supported by the NIGMS for a number of years. Gradually their collaborative studies focused on a particular steroid chemical, cholesterol, and they discovered a mechanism that controls its metabolism. Since such basic studies of cholesterol are critical to an understanding of, and the development of treatment regimens for, atherosclerosis and other cardiovascular disease, their research, originally supported by NIGMS, has been supported by the National Heart, Lung, and Blood Institute in recent years. Dr. Lenfant and I are pleased to thus illustrate the importance of all units of NIH in the continuum of biomedical research activities.

Pharmacological Sciences Program - Biorelated Chemistry

A field which has greatly contributed to our fundamental biomedical knowledge is chemistry. In 1985, the National Academy of Sciences (NAS) published a survey of Opportunities in Chemistry in which it outlined the past contributions of this field and the future advances which may lead to better health. As stated in the NAS report:

> Chemistry in the next decade will contribute to the solution of some of contemporary biology's most important problems. . . . Ultimately, our ability to control complex biological events will depend upon understanding at the molecular level. . . . Chemistry research relevant

to the NIH mission concentrates largely in the National Institute of General Medical Sciences.

Much research in chemistry involves efforts to relate the physical and chemical behavior of organic compounds to their molecular structure. It deals with the pathways by which chemical reactions occur. Over the years, the NIGMS has supported many chemists working in this area, including Nobel Laureates Drs. Herbert Brown, Roald Hoffmann, and Henry Taube. All of them helped to elucidate chemical reactions which are of importance to both health-related areas and industry.

Another significant area of chemistry is the synthesis of biologically important and useful substances which lead to products of far greater purity than can be obtained by starting with natural materials. Such synthesis has led and will lead, with even greater rapidity, to the development of new and more active therapeutic agents. For example, a chemist at the University of California in Berkeley has developed more efficient and direct methods for the total laboratory synthesis of steroids, a class of compounds that includes the anti-inflammatory agent, cortisone, and sex hormones, such as estrogen and progesterone. Steroids are chemicals in which atoms are arranged in a complex cyclic configuration. The team at Berkeley, using chemicals containing metals such as cobalt, has achieved the ability to catalyze or speed up the assembly of the needed atoms in cyclic fashion, directly and efficiently. This approach has been shown to be very versatile and is being used industrially to produce vitamin B_6 (a vital dietary constituent), as well as various pharmacologically active cyclic compounds, such as synthetic estrogens and corticosteroids.

Genetics Program

Another chemist, Dr. Jacqueline Barton of Columbia University, is designing molecules that can recognize and insert themselves into specific sites of the deoxyribonucleic acid (DNA) molecule, thus changing its structure. This may lead to the development of new cancer chemotherapeutic agents as well as a greater understanding of gene expression.

Identification of specific sites of expression of particular genes has permitted researchers to alter these genes, using a method called "site- directed mutagenesis." This technique first involves a determination of the sequence of the nucleotide building blocks of the gene being studied. Next, copies of these sequences are synthesized in the laboratory, except that each copy has a small altered fragment which causes a change, or mutation, at a specific site. These altered sequences are then combined with the host DNA, using recombinant DNA technology. What this does is to replace a normally occurring genetic instruction with another which is man-made. This new instruction may be designed to produce a specific protein--one which geneticists can tailor to particular requirements, for example, for the production of therapeutic products which may serve as anti-viral or anti-cancer agents.

Biophysics and Physiological Sciences Program

Furthermore, site-directed mutagenesis has been used extensively by biophysicists to test their theories as to the relationship of the structure of a particular protein to its function. If a mutation is produced at a single specific site on the gene coding for a protein, an altered protein is produced. Biophysicists thus can determine the relation of the altered protein structure to abnormal function; for example, the abnormal hemoglobin present in sickle cell disease or thalassemia.

This methodology is but one of a number of new techniques which, like highly sophisticated research instruments, have been developed by NIGMS grantees in order to permit the scientific advances which we have called the "biological revolution." Among these are rapid DNA sequencing, the chemical synthesis of nucleotide sequences, methods to isolate very large DNA fragments, as well as computer programs to identify these segments. Another new technique, two-dimensional nuclear magnetic resonance, has the potential to determine the positions of specific atoms in large molecular complexes of proteins and nucleic acids, which are the very "stuff of life."

Cellular and Molecular Basis of Disease Program

Scientists use these techniques, X-ray crystallography, recombinant DNA technology, and site-directed mutagenesis, along with disciplines such as chemistry and genetics, to gain more and more understanding of how the cell functions. What stands out is the dramatic expansion of the use of all these tools to learn about the organization of cells into tissues and organs. Fundamental questions still exist about how a multicellular organism develops. What is the time sequence of developmental events? How are they controlled? How do individual cells coordinate their behavior so that each plays its proper role at the proper time?

Recently, and very surprisingly, it has become clear that some answers to these questions may come from studies of groups of single-cell organisms, bacteria. It turns out that a certain type of bacteria called Myxobacteria undergoes, during its life cycle, primitive differentiation by single cells coming together into a multicellular form and that this is based on the exchange of chemical signals between the cells. These important studies by Dr. Martin Dworkin of the University of Minnesota and Dr. A. D. Kaiser of Stanford University, among others, make use of the remarkable genetic, biochemical, and molecular manipulations and analyses that are possible today, in order to determine what intercellular chemical signals are needed to coordinate the development and differentiation of the multicellular state. By making mutants of Myxobacteria and using recombinant DNA technology, Dr. Kaiser has been able to find that certain chemicals are required and must be available to all the individual bacterial cells in order for multicellular development and differentiation to take place. If the chemicals are not available to the mutant bacterial cells, such development is inhibited. Dr. Kaiser has found that this simple bacterial model is very easily manipulated and may well become the first system of multicellular development to be fully understood in terms of genetic and molecular mechanisms.

Research Training

It is abundantly clear that fundamental research is a most remarkable endeavor and one which is very rapidly providing answers to critical problems of health and disease. This enormous leap forward through the development of new technologies and instrumentation has been made possible by the creativity and continuum of endeavors of a broad spectrum of researchers. The NIGMS research training programs have had a very large role in the preparation of superb scientists at universities throughout the country, scientists who have made, and are continuing to make, important advances both in untargeted basic research and in targeted studies such as those now being done by Drs. Brown and Goldstein, this year's Nobel Laureates. Indeed, while many NIGMS research grantees were supported under the Institute's research training programs, about one-half of those supported in NIGMS predoctoral training programs now are doing research which is supported by other, categorical institutes of NIH. Furthermore, as you know, a study by the National Academy of Sciences has shown that the young men and women trained in NIGMS-supported predoctoral programs have been more productive scientists than are those who did not receive NIH research training support. Of particular note is the Medical Scientist Training Program, which provides students with research training for the combined M.D.-Ph.D. degree. Individuals with this combined degree are among the most successful in obtaining research grant support from NIH.

Minority Access to Research Careers Program

One specialized training program about which I have told this Committee in past presentations is the Minority Access to Research Careers (MARC) Program. I am pleased to tell you that this year an evaluation of the MARC Honors Undergraduate Research Training Program has been completed by the National Academy of Sciences Committee on National Needs for Biomedical and Behavioral Research Personnel. The study found that MARC honors students are talented and highly motivated and that many of them would have been unable to finish their college curriculums without support from the MARC Program. Seventy-six percent of the MARC trainees who have graduated are enrolled in advanced graduate or professional studies. The percentage of biology majors at schools which have MARC Honors Programs has increased, and there are higher rates of bachelor's degrees earned in biology than previously. I have copies of this report available for members of the Committee.

I hope that I have conveyed some of the excitement of the advances in fundamental biomedical research, which are continuing to have an enormous impact on our understanding of ways to maintain and improve the health of the people of the world. The pace of discovery has been increasing but is far from its peak. There is so much yet to learn. The programs of NIGMS are aimed at providing the research manpower to keep up the momentum and at advancing knowledge of the fundamental cellular, molecular, chemical, and genetic processes so essential to developing better ways to prevent and treat disease.

Mr. Chairman, the 1987 budget request for this Institute is $471,533,000. I shall be pleased to answer any questions.

KIRSCHSTEIN, DR. RUTH L.
Director, National Institute of General Medical Sciences

October 12, 1926. Brooklyn, New York

Education: A.B., magna cum laude, Long Island University, 1947. M.D., Tulane University School of Medicine, 1951.

Professional History: 1951-52, Internship, Medicine and Surgery, Kings County Hospital, Brooklyn, N.Y. 1952, Assistant Resident, Pathology, Veterans Administration Hospital, Chamblee, Ga. 1952-54, Resident, Pathology, Providence Hospital, Detroit, Mich. 1954-55, Trainee of National Heart Institute and Instructor in Pathology, Tulane University School of Medicine. 1956-57, Medical Officer, Resident in Pathology, Clinical Pathology, Clinical Center, NIH. 1957, Medical Specialty Board Certification, Pathology (anatomic and clinical pathology). 1957-60, Medical Officer, Pathologist, Laboratory of Viral Products, DBS, NIH. 1960-62, Chief, Section of Pathology, Laboratory of Viral Immunology, DBS, NIH. 1962-64, Assistant Chief, Laboratory of Viral Immunology and Chief, Section of Pathology, DBS, NIH. 1964-65, Acting Chief, Laboratory of Pathology, DBS, NIH. 1965-72, Chief, Laboratory of Pathology, DBS, NIH. 1971-72, Assistant Director, Division of Biologics Standards, NIH. 1972-73, Acting Deputy Director, Bureau of Biologics, FDA. 1973-74, Deputy Associate Commissioner for Science, FDA. 1974-present, Director, National Institute of General Medical Sciences, NIH.

Professional Organizations: American Association of Immunologists; American Association of Pathologists; American Society for Microbiology; Institute of Medicine, National Academy of Sciences.

Committee Memberships: Invited member of World Health Organization Expert Group on International Requirements for Biological Substances; Geneva, Switzerland, 1965 and 1971. Invited consultant to World Health Organization concerning problems related to the use of Poliovirus Vaccine, Live, Oral; Geneva, Switzerland, 1967. Member, Primate Research Centers Advisory Committee, Division of Research Resources, NIH, 1971-1975. Member, National Commission on Diabetes, 1975. Member, National Commission on Arthritis and Related Musculoskeletal Diseases, 1975. Chairperson, NIH Grants Peer Review Study Team, 1975-1976. Chairperson, PHS Genetics Coordinating Committee, 1976-1979. Member, Fogarty International Center Scholars-in-Residence Advisory Committee, 1977-1982. Member, NIH Coordinating Committee on Manpower, 1978-1983. Chairperson, PHS Task Force on Women's Health Issues, 1983-1984. Chairperson, PHS Coordinating Committee on Women's Health Issues, 1984-present. Member, NIH Advisory Committee for the IOM Study of the Organizational Structure of the NIH, 1983-1984. Member, HHS Executive Development Board, 1985-present.

Honors, Awards: Elected to Institute of Medicine, National Academy of Sciences, 1982. Doctor of Science, Honoris Causa, The Mount Sinai School of Medicine, 1984. Honorary Doctor of Laws, Atlanta University, 1985. DHEW Superior Service Award, 1971. PHS Superior Service Award, 1978. Presidential Meritorious Executive Rank Award, 1980. PHS Equal Opportunity Achievement Award, 1983.

PHS Special Recognition Award--group award to PHS Task Force on Women's Health Issues (Dr. Kirschstein, Chairperson), 1985. Distinguished Executive Service Award of the Senior Executive Association, 1985. Presidential Distinguished Executive Rank Award, 1985.

MANDATING NUMBER OF GRANT AWARDS

Mr. NATCHER. Thank you very much, Dr. Kirschstein.

Now, you have been at NIH some time, and you have appeared before our committee on many occasions. You are familiar with last year's controversy over the number of research grants to be funded out of the 1985 appropriations.

You know that in response to the proposal to stretch a portion of the 1985 appropriation over two years, thereby reducing the number of grants to be funded, the committee was forced to specify the number of competing grants at 6200 in appropriation language.

In the 1986 Act, we felt that we had to do this again. Now, we have before us a proposal to eliminate the legislative requirement to fund no fewer than 6100 competing grants in 1986.

We also have before us a budget proposal to include in the 1987 bill a requirement that no fewer than 19,400 competing and non-competing awards be funded by NIH and the Alcohol, Drug Abuse and Mental Health Administration in 1987.

Dr. Kirschstein, tell us, if you will, please, how you feel about the advantages and disadvantages of including, number one, the number of competing research grants or, number two, the total number of grants, competing and non-competing, in the Appropriations Act.

How do you feel about it, Doctor?

Dr. KIRSCHSTEIN. Mr. Chairman, the new stabilization policy of the Department, which would specify the total number of research grants rather than specifying the number specifically for new and competing research grants would provide some needed stability for the research community.

However, there would be some fluctuation from year to year in the number of new and competing grants. Dependent on which particular year an individual applied for a new or a competing renewal grant such a fluctuation might affect that particular individual, either adversely or positively.

Overall, however, I think that knowing that there will be stabilization of the total number of grants could have a very positive effect.

Mr. NATCHER. Thank you, Dr. Kirschstein. Last year this subcommittee decided the way to handle this bill as far as NIH is concerned is to put in enough money in the bill and then fix the number, as far as new grants are concerned. This was our idea.

MERIT AWARD

Dr. Kirschstein, describe the new Merit Award.

Dr. KIRSCHSTEIN. The new mechanism that NIH proposes, called the Merit Award, is an award for a reserach project to very meritorious investigators, which would provide between 5 and 10 years of support for such individuals as a result of a recommendation made by the advisory council of each particular Institute.

It would be a mechanism by which well-known, established investigators could receive longer periods of support than they do currently in order to allow them to continue to do highly meritorious research without having to be concerned about making applications at repeated short intervals.

Mr. **Natcher**. Thank you.

What are the reasons for creating this new type of award at this particular time, Doctor?

Dr. **Kirschstein**. The proposal to create a Merit Award is an NIH initiative and I will give you my comments on it, and then perhaps Dr. Wyngaarden might like to add his.

I believe the reasons for creating or planning such an award relate to discussions that were held a year or so ago, at the NIH Director's Advisory Committee, which met to consider the length of research grants and the entire peer review system.

This Committee felt that there ought to be a mechanism by which established highly meritorious investigators could continue their research endeavors, and expand their horizons without having to reapply for grant support every three or so years.

This would give such investigators a feeling of stability and an opportunity to undertake some projects that they might not otherwise consider doing.

Dr. **Wyngaarden**. We did examine the entire extramural award system. We looked at three major issues; that is, the matter of the first-time investigator, the mid-career investigator, and those having very high productivity, as well as other ways in which we could make the system more efficient, that is, the whole process of review at the study section and council level. The Director's Advisory Committee agreed with our concerns and made some recommendations, and this proposed Merit Award grew out of that conference. This is a device to provide longer-term support for exceptional mid-term scientists. The scientists that would be eligible would have at least three awards from us, over a 10-year period and have been doing research in the very high priority area. It must also be the judgment of the council that their research would be likely to be highly productive for some period into the future. The award would be made in two parts, for up to a 10-year award. Mechanically, it would be viewed as two consecutive awards with less than the usual requirements laid on the investigator during the renewal process.

For example, in the fourth year, the investigator would file a summary progress report rather than a voluminous re-application, and if everything was still highly satisfactory, that person would receive, in effect, an extension. It would be counted as a competing renewal grant, however, so our commitment base, namely the number of extant awards, would not grow out of control.

This would have almost no effect on the commitment base, but would simplify the procedure for those individuals who undoubtedly will be approved anyway.

Mr. **Natcher**. Will all Institutes make these awards?

Dr. **Wyngaarden**. Yes.

Dr. **Kirschstein**. Yes, sir.

Mr. **Natcher**. How many such awards will be made?

Dr. **Kirschstein**. The award mechanism has not yet been implemented, and specific guidelines, I think, are in the process of being developed.

I would anticipate that there would be very few awards made during the first or second year, and that NIH would gradually award a more significant number as time goes by.

We anticipate that the advisory councils will probably look at these awards very carefully.

As the National Institute of General Medical Sciences has been planning for such awards, it is the feeling of its advisory council that the investigators to be considered for such awards, should have had previous NIGMS support for at least 10 years.

NEGOTIATED DIRECT COST REDUCTIONS

Mr. NATCHER. The budget, as you know, requires negotiated reductions in direct costs of noncompeting and competing research grants in both 1986 and 1987.

How large, percentage-wise, will these reductions be in research projects funded by your Institute?

Dr. KIRSCHSTEIN. For non-competing awards, at the FY 1986 sequestration level the reductions will be approximately 6 percent of the direct costs. For competing awards, these reductions will be approximately 9 percent. In FY 1987, these reductions would average 12 percent for noncompeting and 11 percent for competing awards. We are, however, looking at these awards and discussing them individually with grantees in an attempt to take into consideration factors that perhaps we at NIH don't know about that may be of particular concern.

Mr. NATCHER. Some Institute Directors have advised us that rather than making negotiated reductions in excess of 10 percent, it would be better not to make a grant at all. Do you agree with that, Doctor?

Dr. KIRSCHSTEIN. There is no question that once one begins to have to negotiate more than 10 percent below the very carefully determined budget for a grant—a budget that the initial review group or study section has put together—there will be a serious adverse effect on the work that an investigator is able to do.

It may require that fewer personnel be used. There may be supplies that cannot be provided. So it is correct to say that it would be very difficult for grantees to deal with budget cuts of 10 percent or more.

COMMENTS FROM PRESIDENT'S SCIENCE ADVISOR

Mr. NATCHER. Dr. Kirschstein, last year when we were in the middle of the controversy over the program level for competing research grants for fiscal year 1985, a letter signed by the President's Science Advisor appeared in the May 30 issue of the *New England Journal of Medicine*, which seems to have been written as a defense of the budget proposal to fund 5,500 competing research grants in 1985, instead of the 6,500 which Congress thought it had approved.

Our committee members have been here long enough, as you know, Doctor, to know that documents written in defense of budget proposals most times must be taken with a grain of salt.

However, this letter is in a different category, because, one, it is signed by the President's Science Advisor; two, it appeared in one of our most prestigious scientific journals; and three, it casts doubt on the quality of the research sponsored by NIH.

Some of the allegations made in the letter are that, (1) the concentration on the number of competing awards prevents funding projects for a longer period, such as five to seven years.

(2) The emphasis on competing projects discourages funding of other mechanisms such as specialized centers of research.

(3) Congressional earmarking diverts large chunks of the NIH budget from more scientifically promising endeavors.

(4) 25 percent of the NIH budget is directed by Congress toward specific diseases, projects and programs, many of which are funded even though they have quite poor scientific ratings.

(5) Excessive Congressional directives are undermining peer review.

Dr. Kirschstein, do you think there is merit in any of these allegations? And if so, Doctor, tell us which ones, or one. Pick out any one of them, Doctor.

Dr. **Kirschstein**. Mr. Chairman, I think that the record of NIH speaks for itself, and particularly the record of the National Institute of General Medical Sciences. I have been delighted over the 12 years that I have been the Director of NIGMS that the members of this committee have understood full well the importance of the fundamental undifferentiated, untargeted research that NIGMS supports, and have realized that this type of research is absolutely essential as an underpinning for all the activities of the other Institutes.

The research supported by this Institute is of excellent quality, and the research applications that we receive are truly excellent. Indeed, we cannot, at the moment, under the exigencies of the budget—which I fully understand—support all of the excellent, important, fundamental research which seeks NIGMS support.

Mr. **Natcher**. All right.

Mr. Conte, I yield to you.

RESEARCH AREAS AFFECTED BY CUTS

Mr. **Conte**. Doctor, it is good to have you here again, and my congratulations as well for receiving a Presidential award for distinguished service.

I was down at the Department the other day, and there was a big poster with your picture on it announcing the award. Obviously they are proud of you, and so are we.

Doctor, looking at this chart I have here, under the revised budget request for fiscal year 1986, you would lose about 170 competing grants from the level funded in fiscal year 1985, and you would lose an additional 130 in fiscal year 1987. That is a decrease of 300 competing grants in two quick years.

What areas of research would be hardest hit by this kind of cut, and what possible repercussions will it have for our research efforts in the years to come?

Dr. **Kirschstein**. The decreases you mention would be felt in all our programs. However, since about two-thirds of the research grants that we award are in the Institute's cellular and molecular basis of disease and genetic program—two areas where the science is moving very rapidly—those are the areas that would be hurt the most.

DOLLARS NEEDED FOR COMPETING AWARDS

Mr. Conte. How much would we need to add to your 1987 request for new and competing grants to keep you at a level equivalent to the one this subcommittee fought so hard for in 1985?

Dr. Kirschstein. Since the Institute's FY 1987 budget provides for 689 new and competing awards, compared to 987 in FY 1985 we are short about 298 new and competing awards.

Mr. Conte. How many millions?

Dr. Kirschstein. An additional 298 new and competing awards, awards which will require $48 milion more.

Mr. Conte. $48 million?

Dr. Kirschstein. Yes.

ELIMINATION OF RESEARCH CENTER GRANTS

Mr. Conte. The justifications show that you will lose one research center grant to the Gramm-Rudman-Hollings sequestration in fiscal year 1986, and an additional four under the budget request for fiscal year 1987.

What centers does the Institute currently support, and which ones would be eliminated in 1986 and 1987?

Dr. Kirschstein. We support research center grants in a number of areas, pharmacological sciences, anesthesiology, burn and trauma research, genetics, and molecular pathology, the latter being the cellular and molecular basis of disease program.

In FY 1986, the Institute will eliminate a genetics research grant. In 1987, under the President's request, one center in pharmacological sciences, one in burn and trauma research, and one in genetics would be eliminated.

Mr. Conte. Are these centers a particularly low priority of the Institute?

Dr. Kirschstein. The highest priority of an Institute such as NIGMS is to support individual investigator-initiated research grants, the activity in which this committee has been particularly interested. There are, however, certain important aspects of the research center grants that our Institute supports that we think are important. The research centers that we support take the fundamental research that is done through the individual research grants, and bring it closer to the clinical arena.

They are bridging grants; to a great extent they bridge the gap between basic research and clinical research.

In the burn and trauma research centers, this is particularly important, because of the need to apply what we have learned about the fundamental body injuries and the total body response to burn and trauma. It is important to apply this to patients and sometimes important discoveries come out of such research. For example, at the Burn and Trauma Center at the Massachusetts General Hospital, under Drs. Burke and Yannas, the very important artificial skin was developed, and is now being used in eight burn centers throughout the country.

Mr. Conte. That center would be closed?

Dr. Kirschstein. That is one of the centers that could be affected.

Mr. **Conte**. Clinical work goes on there was well as basic research, is that correct?

Dr. **Kirschstein**. Yes sir, clinical studies, as well as basic studies.

OTHER RESEARCH

Mr. **Conte**. Staying on that same page of your justifications, under the heading of "Other Research" you have a category called "Other". I assume most of that is R&D contracts, is that correct?

Dr. **Kirschstein**. The subcategory of "Other" under the heading, Other Research includes funds for the support of research conferences and scientific meetings, as well as funds for the peer review system.

Mr. **Conte**. According to the justification you will go from 21 of these projects under our 1986 appropriation to just two in 1987. What are you cutting out? Are we losing valuable information and research here?

Dr. **Kirschstein**. We would eliminate support for scientific conferences.

Mr. **Conte**. No research?

Dr. **Kirschstein**. That line item does not include funds for research, per se.

HUNTINGTON'S DISEASE STUDY

Mr. **Conte**. Doctor, as you know, over the years I have been following your cooperative work with the Neurological Institute on Huntington's disease. That work led directly to the discovery of the genetic marker for Huntington's. Will you be able to maintain your half of this work, including the cell bank, under the fiscal year 1987 request?

Dr. **Kirschstein**. Yes, we will continue to maintain those endeavors. The cell bank will be supported at a somewhat lower level than it has been in the past, but it will be maintained.

At the moment, the entire collection of cell lines from patients with Huntington's disease is in the cell bank.

These cell lines have been characterized, and now it is a matter of maintenance for investigators.

RESEARCH TRAINING CUTS

Mr. **Conte**. Your justifications show that in fiscal year 1987 individual training awards will drop by about 150, and institutional training awards by about 300. You and I have talked in the past about the major role your Institute plays both in pre-doctoral training and NIH-trainees overall. Will you be able to keep up with your historical role as one of the main training forces at NIH with these kinds of decreases?

Dr. **Kirschstein**. The fiscal year 1987 budget for research training will allow NIGMS to meet all its commitments, but will not permit the award of any new training grants or any new individual fellowships. In part, this is related as you probably know, to the fact that the tuitions at most universities are rising. As a result, each training grant is costing more than it did in the past.

The role of NIGMS in the past has been to support about two-thirds of the pre-doctoral trainees that NIH as a whole supports. That portion in fiscal year 1987 will drop to a little bit less than 50 percent.

Mr. CONTE. Doctor, I saw a recent National Science Board report covering the years 1977 to 1984 showing an overall decrease in NIH support for science and engineering graduate students over those years. Doctor, you have been Director of the Institute since 1974; is that the same basic trend you have seen, and shouldn't this era of boom in biomedical research mean that we should be increasing the numbers of young scientists?

Dr. KIRSCHSTEIN. I have seen the same trend. The National Academy of Sciences, as you know, Mr. Conte, has a committee that recommends to NIH, on a recurring basis, the number of trainees that it feels is appropriate in the basic biomedical sciences, the clinical sciences, et cetera.

Currently, the number of trainees that the NIGMS can support, at the pre-doctoral level in the basic biomedical sciences, is about 800 less than that recommended by the National Academy of Sciences.

Mr. CONTE. That is quite a lot.

All right, I have consumed my ten minutes.

Mr. NATCHER. Mr. Stokes.

EFFECTS OF SEQUESTRATION IN 1986

Mr. STOKES. Thank you, Mr. Chairman.

Always nice to see you before our subcommittee. I notice that $22.1 million is your Institute's share of the 1986 Gramm-Rudman reductions. What research and research training activities would have been conducted with these funds?

Dr. KIRSCHSTEIN. Mr. Stokes, in the area of research training, the dollars under sequestration are reduced by about $2.5 million, and the number of trainees is reduced by 131.

In the area of research grants, while the dollars have been decreased, the number of new and competing research grants remains the same, because, as you know, it is the NIH position that since this committee and the Congress mandated the number of new and competing research grants in law, this number must be maintained.

RESEARCH TRAINING

Mr. STOKES. I see. Your budget justification states that the role of the NIGMS in the training of future researchers is vital to meet the needs of academic research and the rapidly expanding biotechnology industry. But, I notice that you will be supporting only 2,797 trainees in fiscal year 1987, 311 fewer trainees than will be supported in fiscal year 1986 and 649 fewer trainees than were supported in fiscal year 1985.

How then do you explain that statement in your budget justification?

Dr. KIRSCHSTEIN. Mr. Stokes, it is true that the Institute feels that the trainees we support are of vital importance, both in academia and in the burgeoning biotechnology industry. We will be supporting far fewer trainees, but we will, through the peer review system and with the advice of the National Advisory General Medical Sciences Council, assure that we support students of very highest quality.

Mr. STOKES. I notice that your budget for research training would drop from $57.7 million in 1986 to $52.9 million under the fiscal year 1987 budget request.

As you know, the Institute of Medicine's 1985 report on personnel needs and training for biomedical and behavioral research states, "It is the committee's view that training funds should not be further reduced."

Do you agree with that conclusion?

Dr. KIRSCHSTEIN. In an ideal world, yes.

Mr. STOKES. What share of all NIH training grants are administered by your Institute?

Dr. KIRSCHSTEIN. About one-third of all the funds that NIH provides to research training are administered by NIGMS. The Institute has been predominant, in the past, in the area of pre-doctoral training. In addition, a very large number of individual post-doctoral fellowships are supported by NIGMS.

MINORITY ACCESS TO RESEARCH CAREERS PROGRAM

Mr. STOKES. Tell us what you are doing to increase the number of minorities supported through institutional training grants that go to non-minority institutions.

Dr. KIRSCHSTEIN. There are several things that the National Institute of General Medical Sciences is doing in that regard.

First of all, as you know, for the last eleven years, the NIGMS has had its MARC, Minority Access to Research Careers program, which has a number of components. Perhaps the most significant one of these is the Honors Undergraduate Research Training Program. Under this program, honors students in the junior and senior years of undergraduate education are supported to take special courses, as part of enhanced curricula, to major in the biological and related sciences, to engage in research training both at their home institutions, which are the schools that have significant numbers of minority students, and at other institutions where they can work with some of the outstanding researchers throughout the country.

In supporting this program, the Institute has provided assistance to a large number of students who are now prepared to go on to graduate school and graduate education.

In addition, by providing for outside research opportunities for these students during summers or other off semester periods, NIGMS has given the majority institutions an opportunity to find out how good these students are, and very often they will then take them on as graduate students.

Furthermore, NIH has put out a memorandum to the program directors of all NIH-supported training programs at majority institutions, reminding them of their responsibility to attempt to recruit individuals who are minorities, and also, has asked—and this is going to be instituted during the next council rounds—the National Advisory Councils to pay particular attention to whether training grant program directors have indeed, looked for minority students.

Finally, once a year, NIGMS sends out a letter to the program directors of all our training grants at the majority institutions informing them about the MARC program, and suggesting to them that they look at the students graduating from MARC programs. We also suggest that they contact the program directors of the MARC undergraduate research training programs, in order to recruit students. In addition once a year, we hold a MARC honors undergraduate student conference, at which the students have an opportunity to meet faculty from majority institutions and present their research projects to them.

During this conference, they learn how to apply and what the requirements are for entrance into graduate school. We think that this has been, and will be even more in the future, a successful endeavor.

MARC PROGRAM BUDGET

Mr. STOKES. You have talked about the MARC program. I am pleased to note that funding for the MARC program was not reduced under the fiscal year 1986 Gramm-Rudman reductions. Nevertheless, can you tell me why the MARC budget is slated to drop by $884,000 in fiscal year 1987?

Dr. KIRSCHSTEIN. The Institute, being deeply committed to the MARC program, made a decision that the reductions in research training required under sequestration in 1986 would not be taken from the MARC program, but would be taken from the other research training activities.

The fiscal year 1987 budget for research training is $52.9 million, which is almost $5 million less than the appropriation in 1986, and $3 million less than the total research training budget under sequestration.

With this severe reduction, it was no longer possible to protect MARC, and we found it necessary to make an appropriate reduction in the MARC program budget.

Mr. STOKES. How is this reduction going to affect the 1987 program?

Dr. KIRSCHSTEIN. The total number of trainees and fellows supported by the MARC program for fiscal year 1985, and the number planned in fiscal year 1986, would be 478. Under the President's proposed fiscal year 1987 budget, that number would be reduced to 395, a reduction of 83.

MARC AWARDS UP FOR RENEWAL

Mr. STOKES. How many of the MARC institutions will be submitting competing renewal applications in 1987?

Dr. KIRSCHSTEIN. A very large number. The MARC undergraduate training program started in 1977, two years later than the passage of the National Research Service Act. Thus, MARC training grant awards are out of phase with most of the training grants supported by the other programs of the NIGMS.

These grants are awarded for 5-year periods, and thus, a very large number of competing renewals in the MARC program are expected in 1987.

There were, you remember, Mr. Stokes, 12 original grants given to institutions under the MARC program, so those, at least, and probably several more will be up for renewal in 1987.

Mr. Stokes. Please provide for the record a list of those institutions.

[The information follows:]

MARC Program

Institutions expected to submit competing renewal applications in 1987 for honors undergraduate research training awards

Institution	City/State
Medgar Evers College	New York, New York
Benedict College	Columbia, South Carolina
Tougaloo College	Tougaloo, Mississippi
Texas Southern University	Houston, Texas
Talladega College	Talladega, Alabama
Atlanta University Center	Atlanta, Georgia
New Mexico State University	Las Cruces, New Mexico
Jackson State University	Jackson, Mississippi
Prairie View A&M University	Prairie View, Texas
Alabama A&M University	Normal, Alabama
Morgan State University	Baltimore, Maryland
Central State University	Wilberforce, Ohio
Wayne State University	Detroit, Michigan

Mr. Stokes. Thank you, Mr. Chairman.

Mr. Natcher. Mr. Early.

NUMBER OF COMPETING GRANTS

Mr. Early. Doctor, it is a pleasure to have you back. In my opinion, you are probably one of the most professional of a group of professionals out at NIH.

Following Mr. Conte's questioning, in 1985, I understood you to reply that you funded 987 new and competing grants.

Dr. Kirschstein. That is correct.

Mr. Early. The proposed budget is going to fund 298 grants less?

Dr. Kirschstein. Yes, sir. The President's 1987 budget provides for 689 competing research project grants, 298 fewer than in 1985.

Mr. Early. That is almost a 300 grant reduction. In your 12 years as Director, Doctor, what is the largest reduction you've ever had in a two-year period, since 1974?

Dr. Kirschstein. I would have to find that for you for the record, but it is a very low number, sir.

Mr. Early. Supply it for the record.

[The information follows:]

Largest Reduction in Number of NIGMS Competing Research Project Grant Awards Over a Two-Year Period, 1974-1987

The NIGMS supported 1,020 new and competing research project grant awards in 1979. This dropped to 711 such awards in 1981, a reduction of 309 awards over a two-year period—the largest two-year reduction between 1974 and 1987. The reduction of 298 new and competing awards from 1985 to 1987 would represent the second largest such reduction.

Mr. **Early**. Would you also go back to, you started out there 30 years ago as a trainee, go back to 1955 or 1956 and supply for the record the largest number of grant reductions in any two-year period.

[The information follows:]

LARGEST REDUCTION IN NUMBER OF NIGMS COMPETING RESEARCH PROJECT GRANT AWARDS OVER A TWO-YEAR PERIOD, 1963-1987

The NIGMS was formally established as a research institute in 1963. A search of Institute records reveals that the reduction from 1,020 new and competing research project grant awards in 1979, to 711 such awards in 1981—a reduction of 309—represents the largest reduction over a two-year period in the Institute's history.

PAYLINE

Mr. **Early**. What was your payline in 1985?

Dr. **Kirschstein**. The NIGMS payline in 1985 was 165.

Mr. **Early**. What will it be in 1987?

Dr. **Kirschstein**. Under the President's budget, we estimate a payline of 150 in 1987.

Mr. **Early**. What percentage of new and competing grants did you fund in 1987?

Dr. **Kirschstein**. 1987?

Mr. **Early**. 1985 first.

Dr. **Kirschstein**. The NIGMS funded 45 percent of its approved applications in 1985. In 1987, it is estimated that this will drop to 31 percent.

GENETICS RESEARCH BUDGET

Mr. **Early**. A 33 percent reduction.

The justification materials for the genetics program indicates that 15 to 20 percent of all health care costs are associated in some way with genetic disease. This strongly suggests that money put into the genetics research could save us more dollars down the road.

Do you agree with that?

Dr. **Kirschstein**. Yes, sir. It is clear that the development of effective methods to deal with genetic diseases could not only save many lives, but also save the health care system a very large sum of money each year, perhaps hundreds of millions of dollars.

Mr. **Early**. In your statement you said that it is one of the most exciting areas of research today. Now from reviewing your budget request, progress in the field of genetics plays an important role in providing needed tools for research across the spectrum.

Yet, you are asking for a 10-percent reduction?

Dr. **Kirschstein**. Mr. Early, one of the things it is very important to realize is that there has been so much progress in genetics research over the last 4 or 5 years, and so many technologies and tools have been developed through studies in genetics, that these findings and technologies are now being used by researchers supported by many other programs. What we have found is that grantees in our pharmacological sciences program, our cellular and molecular basis of disease program, and our biophysics and physiological program are all using the tools that were developed originally in genetics.

Mr. **Early**. That is what is so important about the NIGMS.

In my 12 years on this committee, I've always thought everything started with your Institute.

The only thing that never resulted was the credit for it and that is why I was pleased to see Doctors Brown and Goldstein, both grantees of NIGMS receive these awards.

Now, Doctor, if we go back to this particular 1987 request, we are going backwards with regards to your Institute in my opinion. You are proposing a 10-percent reduction in the budget for genetic research?

Dr. **Kirschstein**. Yes, sir. The proposed FY 1987 NIGMS budget provides $143.3 million for research project grants in the area of genetics. This compares to $161.7 million in the 1986 appropriations bill—a reduction of about 10 percent.

IMPACT OF BUDGET REDUCTIONS

Mr. **Early**. I don't know how we justify, any which way, progress, the potential for progress with this type of request. Talk about AIDS, all the other things—your statement mentions site directed mutagenesis, well, that sounds exciting. Yet, you are coming in here with the biggest reductions NIH has ever suggested before this committee.

In your professional judgment, Doctor, in your professional judgment, at what point do we reach the danger zone where the reductions begin to affect the quality or scope of the research, or have we gone well beyond that danger zone?

Dr. **Kirschstein**. As I told the Chairman before, we feel that when a grantee is asked to take a reduction in the budget for his or her particular individual research grant in excess of 10 percent, it will be very difficult to be able to do important, meaningful work. While research will not cease, the pace of discovery will slow down very considerably.

Mr. **Early**. It is obvious it will not cease.

We are letting it slow down to this degree. If we are going to lead the world at NIH—you started out there prior to 1955 as a trainee, Doctor—have you ever seen institutes with less tools than would be provided in this particular budget? I am not trying to put you on the spot, but it is so obvious. You've got cuts in indirect and direct costs, intramural, training that you have taken. Out of 900 grants, you are going down to 600, that is a 33.3 percent reduction.

In your professional opinion, Doctor, has there ever been less autonomy for the directors than there is out there now? How can you have any?

Dr. **Kirschstein**. Within the constraints of the budget I will try to make the best judgments I can, sir.

Mr. **Early**. I am sure you will. Every director that has come in here, they have come in and stated their case, and it is hard to pull it out of you, a lot harder than it used to be, and that was back when they were trying to level fund you.

ADVANCES IN GENETICS RESEARCH

What kinds of research advances are on the horizons with regards to genetic research?

Dr. KIRSCHSTEIN. There are a number of very exciting areas. As you know, several years ago, we reported, in collaboration with the Neurological Diseases Institute, on the discovery of a genetic marker for Huntington's disease. Now there have been a number of new markers found, one, in particular, for Cystic Fibrosis. What is happening is that, as the scientists are perfecting the techniques of gene mapping, gene walking, gene jumping; as they are perfecting the techniques of using restriction fragment length polymorphisms to look for markers for genetic diseases, they are pinpointing the sites of more and more of those genes that cause diseases.

In addition, there is on the horizon, the possibility of one day inserting specific healthy genes to correct defects which cause certain genetic diseases.

Mr. EARLY. I read that in your statement, and that is how we would address AIDS and other problems.

Earlier, you suggested that you have identified the gene for Huntington's, the marker. Now you are telling us you have identified a marker for CF?

Dr. KIRSCHSTEIN. This particular work was not done by grantees of this Institute, but by people using the techniques developed by our grantees.

Mr. EARLY. It isn't really a sexy, sexy Institute as far as publicity, but probably the most important, always the one I was most comfortable funding because we don't earmark anything with you.

That is the way it is supposed to be. We are earmarking if we make reductions like you are suggesting?

Dr. KIRSCHSTEIN. I would hope there would be some remaining flexibility, Mr. Early.

RESEARCH TRAINING BUDGET

Mr. EARLY. You were a trainee 30 years ago at the Institute. How many trainees did you have in 1985?

Dr. KIRSCHSTEIN. NIGMS provided support for 3,396 in 1985.

Mr. EARLY. How many does this budget propose?

Dr. KIRSCHSTEIN. The Institute's budget provides for 2,797 in 1987.

Mr. EARLY. You told Mr. Conte before, but how does support for trainees in 1987 compare with the recommendations made in the National Academy Report?

Dr. KIRSCHSTEIN. The number of pre-doctoral trainees we would be able to support in 1987 is about 800 less than the National Academy of Sciences has recommended.

Mr. EARLY. Madam Director, I think you are losing all your flexibility, and all your autonomy which was the biggest virtue of the NIH, and with the numbers in this particular 1987 request, Madam Director, it is disturbing. I have a lot more questions.

Thank you, Mr. Chairman.

RESEARCH TRAINING

Mr. NATCHER. Dr. Kirschstein, your Institute is heavily involved in the training of future biomedical research scientists. I believe that you support ⅔ of the pre-Ph.D. research trainees funded by NIH, and ⅓ of all NIH-funded trainees. Your budget shows that the number of trainees supported by your Institute will decline from 3,396 in 1985 to 3,108 in 1986 and to 2,797 in 1987.

For NIH as a whole, the number of trainees supported declines from 10,624 in 1985 to 9,948 in 1986 and to 9,258 in 1987. I am sure we will hear many complaints about these reductions, but I cannot help but wonder whether it is wise to continue training at higher levels, if we are going to continue to support about 18,000 research grants a year.

Can we provide research support for the researchers we are training?

Dr. **Kirschstein**. Mr. Chairman, I do think it is important to continue to provide support for research training, because we are training not only individuals who will be the researchers at universities and research institutions throughout the country, but also individuals who will work for the burgeoning biotechnology industry.

Many of the trainees that are being supported in the fundamental programs at the pre-doctoral level are being sought after by biotechnology companies even before they have developed as fully mature scientists and even before they take their post-doctoral training.

We have heard from a number of people in academia that it is not easy to find post-doctoral fellows in the fields of molecular biology and cell biology because they are being sought by industry; so I do think that by continuing to train individuals, we are satisfying an important need for the country as a whole.

NRSA REAUTHORIZATION

Mr. **Natcher**. The Health Research Extension Act extends the authorizations for support of research training. Does that law make any other important changes with respect to the research training program?

Dr. **Kirschstein**. It provides for several changes, one of which is that a report will be requested from the National Academy of Sciences at least every 4 years, rather than at least every 3 years.

Second, it authorizes for funds for research training in primary care and for research, training in health services research. These are two areas that have not been covered previously under the National Research Services Act.

Mr. **Natcher**. If you will, Doctor, place in the record at this point a summary of the provisions of the new laws which relate to research training.

[The information follows:]

Summary of the Provisions of P.L. 99-158, the Health Research Extension Act of 1985, Relating to NIH's Authority to Support Research Training

Section 487 of the Health Research Extension Act of 1985, signed into law on November 20, 1985, renews for three years the authority of NIH to provide both individual and institutional National Research Service Awards for the support of predoctoral and postdoctoral training related to biomedical and behavioral research. Other key provisions of the law include the following:

Authorization Levels: The new funding authorization levels (including funds for awards provided by other PHS components) are as follows:

	Million
1986	$244
1987	260
1988	275

Individual Awards: Of the amounts appropriated, not less than 15 percent must be made available for awards to individuals.

Institutional Awards: Of the amounts appropriated, not less than 50 percent must be made available for awards to institutions.

Training in Primary Care: Of the amounts appropriated, 0.5% must be made available for research training related to primary care.

Training in Health Services Research: Of the amounts appropriated, 0.5% must be made available for training related to health services research.

Short Term Training: Of the amounts appropriated, not more than 4 percent may be obligated for training of three months or less.

NAS Report: The National Academy of Sciences will be asked to generate a report establishing the nation's overall needs for biomedical and behavioral research personnel and provide related information at least once every four years, instead of once every three years as required previously.

Pay Back Requirement: The new legislation retains the requirement that trainees engage in health research and/or teaching within a reasonable period of time after graduation or repay the Government's investment in their training. However, the law also directs the Secretary of Health and Human Services to conduct a study of the effect of this obligation on the number and quality of the individuals who apply for NRSA awards and the number and quality of persons who engage in health research.

GENETICS RESEARCH ACTIVITIES

Mr. NATCHER. I believe that about 40 percent of your research budget is allocated to genetics. Many, if not all of the other Institutes, now seem to be supporting genetics research. Is there any problem of duplication of effort?

Dr. KIRSCHSTEIN. No, I don't think so.

First, the genetics research that NIGMS supports, as in all the other research areas that we support, is undifferentiated and untargeted. It is not targeted toward particular genetic diseases. It may use some of those genetic diseases as model systems, but most of it is very fundamental research which has led to enormously important discoveries.

The entire technology of recombinant DNA came out of the genetics research supported by NIGMS.

When it is appropriate to concentrate on certain genetic diseases, so as to develop certain technologies, NIGMS does, for example, support the development of the technique of using restriction fragment length polymorphisms. This enabled the markers for cystic fibrosis and Huntington's disease to be found; but the primary research on these diseases is supported by the categorical Institutes.

Furthermore, the staff of my Institute and the other Institutes which are concerned with genetics are in constant communication with each other and exchange information all the time, so that there is no duplication.

Mr. **Natcher**. Tell us how the decision is made as to which Institute supports which research project involving genetics.

Dr. **Kirschstein**. Yes, sir.

Each of the Institutes at NIH, dependent upon its mission as outlined in its enabling legislation prepares what are called "referral" guidelines for the use of the NIH Division of Research Grants, which has the responsibility to refer research grant applications to the appropriate Institutes.

These guidelines are very carefully crafted to assure that they cover the areas in which a particular Institute is interested.

After these guidelines have been prepared, each of the other Institutes is asked to review them to assure that they do not overlap their missions and do not cause problems concerning referral to the various Institutes. In areas where there may be some overlap, dual assignments are made. Thus while a research grant application may be assigned to the National Institute of General Medical Sciences as the primary institute, it may also be assigned to one of the other Institutes on a secondary basis; the latter Institute could make an award if NIGMS did not.

This indicates that NIGMS is the most appropriate Institute but the other one could also be appropriate.

GENE MAPPING

Mr. **Natcher**. Dr. Kirschstein, what is gene mapping?

Dr. **Kirschstein**. Gene mapping is the science by which the location of a particular gene—for example, a disease causing gene—is pinpointed on a chromosome.

There are a very large number of genes, about 100,000, each of which has a particular assignment on one of the 46 human chromosomes.

We do not know the location of most of those genes, but we do know the locations of many more of them than we knew 10 years ago; and each year, more and more of the genes are being pinpointed to a particular location on a particular chromosome. That is called gene mapping.

NUCLEAR MAGNETIC RESONANCE

Mr. **Natcher**. In the past you have supported research on the development of NMR as a diagnostic tool. Other Institutes are doing this, too. How do you divide up your efforts as far as NMR is concerned?

Dr. **Kirschstein**. The development of the instrumentation and the techniques involved in nuclear magnetic resonance were supported by the National Institute of General Medical Sciences. Those techniques are now being used in two different ways. One is to produce an NMR image of a section of the body for diagnostic purposes. That is no longer called NMR imaging but now is called MRI which stands for magnetic resonance imaging.

The other use of this technology is to study molecules and compounds in vivo, in the body. This Institute continues to support the development of both diagnostic and other types of NMR, but once the diagnostic procedures have been worked out, they are being applied by the other Institutes to enhance specific diagnostic capabilities particularly in regard to neurological diseases.

The National Institute of General Medical Sciences supported the early development of nuclear magnetic resonance imaging, for diagnostic purpose by Dr. Paul Lauterbur. Dr. Lauterbur, previously an NIGMS grantee, won the Lasker Award for research in this area in 1984. Those imaging techniques are being supported now primarily by the other Institutes.

Mr. NATCHER. Generally speaking, how much of your budget goes to nuclear magnetic resonance?

Dr. KIRSCHSTEIN. Research activities concerned with nuclear magnetic resonance (NMR) spectroscopy are supported through the Institutes Biophysics and Physiological Sciences Program, which currently has a budget of about $95 million, and I would think that something in the order of $20 or $30 million would be approximately what is being spent on NMR related research.

BURN RESEARCH

Mr. NATCHER. Why is research on burns supported by your Institute rather than one of the Institutes which do research on skin problems?

Dr. KIRSCHSTEIN. The enabling legislation for NIGMS provided two major missions for the Institute. One is the area that we have been emphasizing up to now; namely, the support of basic undifferentiated research. The second is responsibility for the support of research that is within the realm of two or more of the other categorical Institutes.

It was felt from the initial stages of the establishment of NIGMS, and continues to be true, that much of the research in burn injury and trauma involves the entire body, and therefore is of interest to two or more of the categorical Institutes.

When the National Institute of Arthritis, Muscular-Skeletal and Skin Diseases is organized, we may have to have some discussions with that institute's staff in order to determine what overlap areas if any, may exist in regard to burn and trauma research.

ARTIFICAL SKIN

Mr. NATCHER. Dr. Kirschstein, if you will, bring us up to date on the development of artificial skin.

Dr. KIRSCHSTEIN. Yes, sir. There are a number of scientists who have been working on the development of artificial skin for the treatment of severe burns. The most advanced are the activities of Dr. John Burke, from the Massachusetts General Hospital, and Dr. I. Yannas at MIT. They have developed an artificial skin that is made up of two layers. The lower layer is made of collagen fibers from shark connective tissue, while the upper layer is a silicon covering.

Their Stage I artificial skin is placed on very extensive areas of burned tissue shortly after the burn occurs in order to reduce the threat of infection and speed healing. This procedure has been very successful. Indeed, this artificial skin has now been used for several years and is being manufacturerd by Marion Laboratories in Kansas City. Under a new drug application made to the FDA by that company, there are now eight burn centers throughout the United States, one of which is the Washington Hospital Center here in Washington, D.C. Another is the Massachusetts General Hospital where the work was started and then there are six others.

To date about 200 patients have been treated with this Stage I artifical skin. It has been extremely successful in saving lives in covering the burn, and in allowing the patients to heal with minimal contractures and scarring. Doctors Burke and Yannas have now developed a Stage II procedure, in which the original Stage I artifical skin is seeded with basal cells, the cells from the lowest layer of the skin. These are the cells that multiply and eventually form the normal skin. This complex is then placed on the burn wound, allowing the patient's own remaining skin to proliferate and eventually to form a normal cover. Six patients have been studied thus far and the technique seems to be working extremely well.

However, this is still a procedure that is not ready for the kind of expanded trial that the Stage I skin is undergoing.

Mr. NATCHER. All right.

Mr. Conte.

GENE THERAPY

Mr. CONTE. Doctor, we have talked some in past years about genetic research, which your Institute held sole rights on for many years. We have moved a long way in 30 years, and now a lot of the genetic research is conducted at the various other Institutes.

One of the next giant leaps we see coming is some kind of gene therapy, where a normal gene can be injected into the cell to take the place of the faulty gene. Besides all the important ethical questions involved, what technical problems are keeping us from initiating this kind of therapy?

Dr. KIRSCHSTEIN. There are a number of studies being done in model systems for this kind of therapy. One of the most important is being done within the intramural program of the NIH by Dr. French Anderson of the NHLBI. He has had considerable success in his research on a genetic disease with something called adenosine deaminase deficiency, which causes severe immunological defects. He has been working on an approach for replacing the deficient gene with a normal gene in the bone marrow cells of an animal model of this disease.

As I understand it, Dr. Anderson has had considerable success with this technique in mice and has now begun to study a nonhuman primate model. He has found, however, that the expression of the gene is not quite as strong in the primates as it was in the mice. Therefore, until he can refine some of these techniques, he is loathe to consider going further to human studies.

Mr. CONTE. I read in your justifications that 15-20 percent of all health care costs are associated with genetic disease. In your opinion, how long will it be until we see some of this gene therapy in actual use?

Dr. KIRSCHSTEIN. While I think the field is moving very rapidly, and a year or so ago, we would have anticipated that such studies in humans might have begun in a year or so, all sicentists are experiencing problems similar to those of Dr. Anderson. Clearly it will take somewhat longer than we anticipated originally, probably several more years.

RESEARCH ON GENETIC CODE

Mr. CONTE. Doctor, does the recent discovery that the genetic code is not the same for all species present any new challenges to your research work?

Dr. KIRSCHSTEIN. Until recently it was considered that the genetic code was universal to all species. One of our grantees has shown that the three-part codon which usually tells the cells of most species to stop making a protein, means something else in a particular single-cell species. It codes for a specific amino acid instead, in this organism. This is a very unusual phenomenon and we have to investigate it further to see whether there are going to be other changes that might be of significance. It has opened up a new area that we did not really anticipate.

ARTIFICIAL RED BLOOD CELLS

I saw in the justifications that your Institute had helped in the development of prototypes for artificial red blood cells. What impact would this development of prototypes for artificial red blood cells have? What impact would this development have on treatments for burn and trauma victims?

Dr. KIRSCHSTEIN. This research could be of significance to individuals who have severe burns or trauma, and occasionally, to individuals who may need rapid blood transfusions, if it develops appropriately. There is still a great deal of work that needs to be done in this area but such research could lead to a way of providing needed hemoglobin, the protein carrying oxygen, by infusing it into individuals in shock or in need of transfusions without having to use human blood. This might be a rapid way of bringing individuals out of shock. Whether it could ever totally replace human blood transfusions is, I think questionable.

ANESTHESIOLOGY RESEARCH

Mr. CONTE. Under your PS (pharmacological sciences) program you do some research into the effects of anesthesia. What factors influence an individual's reaction to anesthesia?

Dr. KIRSCHSTEIN. There are a number of things that influence an individual's reaction to anesthesia, but interesting enough, one of the factors is genetic makeup. For example there is a disease called malignant hyperthermia in which an individual responds with very high fever under the influence of certain anesthetics. This disease has a genetic basis and we have just learned a little more about it than we knew before. It is very serious and if the very high temperature that a patient develops is not rapidly lowered, he or she may die. So it is very important to understand the mechanisms underlying this condition and other reactions to anesthesia. There are efforts going on in this regard right now.

Mr. CONTE. How can you know when a patient has these genetic problems?

Dr. Kirschstein. That is what we are attempting to find out now. There are certain things to look for, however. For example, if the individual had anesthesia before and had a similar reaction—

Mr. Conte. What are we talking about?

Dr. Kirschstein. We are taking about the use of gaseous anesthesia that an individual would receive to major surgery.

Mr. Conte. How about a spinal?

Dr. Kirschstein. No, the problem only occurs when a general gaseous anesthesia is given.

Mr. Conte. What happens with someone whose never had an operation in his life, what will you do?

Dr. Kirschstein. At the moment, perhaps nothing unless there is a family history. If there is such a history. Studies of muscle tissue removed by biopsy are used to diagnose the condition. However by learning more about this disease by studying the patients who survive, by studying malignant hyperthermia in a modeled system, we hope to learn enough to be able to make some predictions and to plan accordingly.

STRUCTURE OF HUMAN COLD VIRUS

Mr. Conte. Some of the new research you describe in your justifications is aimed at analyzing the structure of molecules. One recent discovery you talk about is work that uncovered the structure of one type of human cold virus. What is the importance of this discovery, and what other diseases might it eventually impact on?

Dr. Kirschstein. I will provide that for the record.

[The information follows:]

Research on the Three-Dimensional Structure of the Human Cold Virus

The physical structures of biological entities, such as viruses, are believed to hold the key to gaining an understanding of how they work. For this reason, the NIGMS provides support for a considerable number of research studies which focus on structural analyses at the molecular level. An expert in this area, Dr. Michael Rossmann of Purdue University, has received support from the NIGMS for a number of years. Recent findings emanating from his research studies, in which he utilized tools developed with NIGMS support, have enabled him to determine, at an atomic level of detail, the three-dimensional structure of the common cold virus. This work is considered to be a major breakthrough, in that it clearly reveals, for the first time, the precise structure of this virus and its relation to its mode of action. Of particular signficiance is the possibility of non-immunological approaches to curing the common cold, as well as other viral diseases. Using the same technique which he developed for his cold virus studies, Dr. Rossmann and other scientists are now considering similar studies on the viruses that cause polio, hepatitus, leukemia, Acquired Immune Deficiency Syndrome (AIS), and foot and mouth disease in cattle.

ARTIFICIAL ENZYMES

Mr. Conte. How close are we getting to producing artificial enzymes, and what effect will their development have on our research effort in general?

You can put that in the record as well.

Dr. Kirschstein. Yes, sir.

[The information follows:]

Progress in Artificial Enzyme Research

Enzymes are proteins which serve to catalyze or "speed up" a host of naturally occurring biochemical processes in the body. Scientist are now able to produce some artificial enzymes with catalytic rates which approximate but do not yet match those of natural enzymes. For instance, scientists currently are developing an artificial enzyme that mimics trypotophan synthetase, the enzyme that catalyzes the synthesis of tryptophan, and amino acid essential in the diet of humans. It is hoped that continued work on those artificial enzymes will soon yield results equivalent to their natural analogs.

Both now, with these less than optimal artificial enzymes, and in the future, when they can completely mimic natural enzyme, there are important uses for artificial enzymes in numerous research fields, but especially in biochemistry. Because the structure of each artificial enzyme is designed by the scientist, it can also be manipulated in order to investigate various hypotheses about how particular configurations bear on whether an enzyme functions normally or abnormally. Abnormal function can lead to serious disorders. Scientists can produce an artificial enzyme model of only that portion of the enzyme molecule which catalyzes a reaction; then they can identify the function of each component of this catalytic site. Alternatively, "designer" enzymes can be synthesized that have binding specificities different from those of natural enzymes. These enable scientists to catalyze reactions with different molecules and end-products than those that normally participate in the reactions.

PRAT PROGRAM

Mr. Conte. Doctor, one of the Institute's programs that you highlight in the justifications is the Pharmacology Research Associate Training, or PRAT program. Can you explain how this program works and why it is such a success?

You can put that in the record, too.

[The information follows:]

Reasons for Success of PRAT Program

The Pharmacology Research Associate Training Program (PRAT) is the only intramural activity of NIGMS. It is a two-year postdoctoral training program to develop top notch leaders in research in the pharmacological sciences and related areas. The vast majority of PRAT fellows move into key positions in academia, industry and government research laboratories. Each year, through a rigorous application, peer review, and interview process, 10 or 11 PRAT fellows are selected from among the 75-100 applicants competing for this special postdoctoral training. Selection criteria include an assessment of each applicant's background in the pharmacological sciences or other basic science field relevant to pharmacology, and an evaluation of the candidate's potential to become an independent, contributing researcher. Those selected for the PRAT Program are matched, on the basis of mutual research interests, with perceptors who are distinguished laboratory scientists, including several Nobel Prize winners, in other NIH institutes or in ADAMHA laboratories. Because there is a shortage of clinical pharmacologists, special efforts are made to place physician-researchers in the Program.

The PRAT Program is a success for several reasons. The rigorous selection process assures that the very best potential researchers participate in the program. While at NIH, PRAT fellows benefit from the excellence of their preceptors and their laboratories, and the opportunities for collaboration and advanced research experience offered in the NIH environment. During their two-year appointments, the PRAT fellows are given a significant degree of freedom to pursue research problems fairly independently. All of these factors account for the impressive success of PRAT fellows in going on to perform research at the cutting edge of pharmacology and related disciplines such as immunology, molecular biology, endocrinology, and chemistry.

As noted in the Institute's justification materials, the PRAT Program was established in 1965; and in the 20 years of its existence, 189 scientists have graduated from the program. Of these, it is known that at least 172 (91 percent) have entered research careers.

Mr. Natcher. Mr. Stokes.

CHROMOSOME WALKING AND GENE JUMPING

Mr. STOKES. Dr. Kirschstein, you have used the term "gene jumping" and "gene walking". What is the meaning of those two terms?

Dr. KIRSCHSTEIN. Actually, I should have used the term chromosome walking, rather than gene walking. As scientists have learned more and more about how to find particular genes at particular sites on the chromosome, they have attempted to improve their techniques. For example, the scientists who have found the marker on chromosome No. 4 for Huntington's disease would like to pinpoint the gene itself. The marker that is associated with that particular gene, of course, is not the same as the gene for Huntington's Disease. It is some distance from the gene. By analyzing all the nucleic acid sequences from the known marker to the point where we expect the gene to be, we hope to be able to pinpoint the location of the gene. They move down or walk down the chromosome analyzing each fragment as they go, in order to find the particular gene being sought.

Chromosome jumping is a little bit different, in the sense that if one knows something about the sequences between the marker and the gene that one is hoping to find, one may be able to jump past certain of the sequences, because they are not of interest, and home-in more rapidly on the particular gene that is being sought.

AVERAGE COST OF MARC TRAINEES

Mr. STOKES. Sounds like fascinating work.

Let me return to the MARC program. What will the average cost per MARC trainee be in 1986 and 1987?

Dr. KIRSCHSTEIN. In 1986, the average cost for all of the MARC trainees and fellows will be about $16,600. In 1987, we estimate that this will increase to $17,900.

Mr. STOKES. Do you have a breakdown in terms of cost per each type of trainee?

Dr. KIRSCHSTEIN. Yes, for the honors undergraduate program, the average cost per student will be $16,400 in 1986, of which about $3,300 will be for tuition. There is a $5,000 stipend, and the institutional costs are about $7,000.

In 1987, the average cost per student will be $17,600, and the tuition goes up to $3,800. The stipend remains the same and the institutional allowance goes up to about $7,700.

IOM/NAS EVALUATION OF MARC PROGRAM

Mr. STOKES. Didn't the Institute of Medicine recently complete an evaluation of the MARC program. Can you highlight the findings of that evaluation?

Dr. KIRSCHSTEIN. At the request of the NIGMS, the Committee of the Institute of Medicine, National Academy of Sciences that evaluates the need for research manpower and personnel needs, did an evaluation of the MARC honors undergraduate research training program. It found that this program has met all the expectations that we had hoped for it; that the students who are training in this program are of excellent quality; that more students at the schools that have MARC undergraduate programs are majoring in biology and science than are students in schools that do not have these programs; that about ⅔ or a little more are going on to graduate education; and that the students seem to have an interest in science and be planning science careers in a way that has not happened before in most minority institutions.

That report has been very pleasing to us. The program has fulfilled all our expectations.

Mr. STOKES. It is certainly good to hear that the MARC Program has had a positive evaluation.

I understand further that the Institute of Medicine recommended that 470 MARC trainees, about the current level, be supported each year for the next several years. Is that correct?

Dr. KIRSCHSTEIN. That is correct.

Mr. STOKES. How much would have to be added to your fiscal year 1987 budget request to implement this recommendation?

Dr. KIRSCHSTEIN. We would have to increase the number of MARC trainees by about 75, and we would have to add about $1.5 million to the MARC budget.

MARC UNDERGRADUATE SCHOLARS CONFERENCE

Mr. STOKES. OK. I note in the justifications that, in 1985, your Institute sponsored the fifth MARC undergraduate scholars conference. Can you either highlight for us today or for the record some of the research conducted by the MARC scholars?

Dr. KIRSCHSTEIN. Let me put that in the record, please, Mr. Stokes.

Mr. STOKES. That would be fine.

[The information follows:]

SOME HIGHLIGHTS OF RESEARCH PROJECT PRESENTATIONS AT THE FIFTH MARC SCHOLARS CONFERENCE

The following are a representative sampling of the 70 research projects presented by MARC scholars and graduates at the fifth MARC Scholars Conference, held at the National 4-H Center in Chevy Chase, Maryland, on November 6–9, 1985:

1. J. Rodriguez-Soto, a graduate of the MARC Program, now at Stanford University, is studying cell motility in a bacterium. This has broad relevance, since several of the blood and tissue cells in man that constitute part of the defense against invading microorganisms are themselves motile. His technically sophisticated approach includes the use of mutants and cloning, with the aim of characterizing the games responsible for cell motility.

2. V. Webster and others at the Charles R. Drew Postgraduate Medical School reported on the function of immune cells in sickle cell anemia. They are following up a preliminary finding that subsets of lymphocytes are present in altered ratios in patients with sickle cell disease.

3. Roger Huey and others at Tougaloo College are working on opiate receptors in the brain, using synthetic analogs to characterize the binding sites of natural neurotransmitters. This is an area of great complexity, but also of great importance in unraveling how the different parts of the brain coordinate their functions.

4. D. M. Avila-Jimenez and others at St. Mary's University in San Antonio are trying to dissect the pathogenic process in cystic fibrosis, and have focused their work on changes in intracellular calcium metabolism. They key finding, so far unexplained, is that lymphocytes and fibroblasts both show deviations from normal in regard to calmodulin content and secretion, but in opposite directions.

5. In their studies of potential inhibitors of inflammation, Sheila Shipsman and colleagues at Pembroke State University in North Carolina, have investigated the effect of a synthetic inhibitor of the enzyme protease. This enzyme is thought to be one of the major causes of tissue damage seen in certain kinds of kidney disease. The compound, called BABIM, has been effective in preliminary studies.

6. Steve Cochrane and coworkers at the City College of New York are trying to isolate a clone coding for the gene for one of the body's key neuroreceptors, acetylcholine. They have made use of a number of modern genetic and molecular biologic techniques to advance their studies and to characterize the gene.

MARC PREDOCTORAL FELLOWSHIP AWARD

Mr. STOKES. Last year I asked you about the fact that the MARC pre-doctoral fellowship award provides a stipend and partial tuition payment, but other predoctoral training programs provide a stipend and full tuition support.

Has anything been done to correct this inequity?

Dr. KIRSCHSTEIN. Yes, sir, for the last year we have been paying full tuition on MARC individual pre-doctoral fellowships.

Mr. STOKES. How many MARC pre-doctoral fellowships will be awarded in 1986 and 1987?

Dr. KIRSCHSTEIN. In 1986, the MARC Program will support 37 pre-doctoral fellowships. In 1987, 27 fellowships will be supported, 10 fewer than in 1986.

MARC PROGRAM SUPPORT FROM OTHER INSTITUTES

Mr. STOKES. You estimated last year that $242,000 would be contributed to the MARC program from other Institutes at NIH. How much was provided in 1985 and give us your estimates for 1986 and 1987?

Dr. KIRSCHSTEIN. In 1985, there was about $200,000 provided by the other Institutes, and we would expect that to continue.

Mr. STOKES. Would you also provide a list for the record of all the Institutes contributing to the MARC program and the amounts contributed in 1985.

Dr. KIRSCHSTEIN. Yes, sir.

[The information follows:]

Contributions to the MARC Program FY 1985

National Heart, Lung, and Blood Institute	$34,000
National Cancer Institute	38,000
National Institute on Aging	5,000
National Institute of Allergy and Infectious Diseases	34,000
National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases	10,000
National Institute of Dental Research	28,000
National Institute of Child Health and Human Development	26,500
National Institute of Environmental Health Sciences	24,000
Total	199,500

MARC BUDGET REQUEST

Mr. STOKES. What was your original request to NIH for fiscal year 1987 funding for the MARC program?

Dr. KIRSCHSTEIN. The original request was $10,776,000.

Mr. STOKES. For the record, indicate how these funds would have been used?

Dr. KIRSCHSTEIN. Yes, sir.

[The information follows:]

ALLOCATION OF MARC PROGRAM FUNDS

[Based on original request—dollar amounts in thousands]

	1987 original request	
	FTTP	Amount
Individual:		
Predoctoral	38	$579
Faculty fellowships	21	588
Visiting scientists	1	30
Subtotal	60	1,197
Institutional:		
Honors undergraduate	448	9,061
Institutional	26	518
Ancillary training activities	0	0
Subtotal	474	9,579
Total	534	10,776

ALLOCATION OF MARC PROGRAM FUNDS

Mr. STOKES. Also for the record, update the table on pages 401 and 402 of last year's hearing record displaying the allocation of MARC program funds.

Dr. KIRSCHSTEIN. Yes, sir.

[The information follows:]

ALLOCATION OF MARC PROGRAM FUNDS

[Dollar amounts in thousands]

	Fiscal year—					
	1985		1986		1987	
	FTTP	Amount	FTTP	Amount	FTTP	Amount
Individual:						
Predoctoral	37	$504	37	$504	27	$398
Faculty fellowships	21	567	21	567	19	506
Visiting scientists	1	29	1	30	1	30
Subtotal	59	1,100	59	1,101	47	934
Institutional:						
Honors undergraduate	387	6,075	393	6,435	324	5,701
Institutional	32	421	26	414	24	353
Ancillary training activities	0	145	0	0	0	78
Subtotal	419	6,641	419	6,849	348	6,132
Total	478	7,741	478	7,950	395	7,066

INTRAMURAL RESEARCH PROGRAM

Mr. STOKES. Can you now give us some examples of the type of research conducted in the NIGMS intramural research program?

Dr. KIRSCHSTEIN. The NIGMS intramural research program is very different from the intramural programs of the other Institutes. Basically, the NIGMS does not have a very large intramural program. What we do have is in the form of support provided through our Pharmacological Sciences Program for 21 or 22 young men and women to train as pharmacology research associates in some of the outstanding intramural laboratories of the other Institutes. They train in laboratories which do research relevant to the pharmacological sciences. NIGMS provides support for them, if they are either already determined to be pharmacologists or if they need broadening in pharmacology or in other scientific disciplines which are related to pharmacology, molecular biology, or important areas of chemistry.

What NIGMS does is to provide these individuals with training stipends, and funds for supplies. Following a competition, the very best ones are chosen and are matched to appropriate preceptors in the intramural programs of the other Institutes.

Mr. Stokes. I would appreciate it if you would provide for the record how much is budgeted for those activities in fiscal year 1987 as compared with fiscal year 1986.

Dr. Kirschstein. I would be pleased to do so.

[The information follows:]

Funds Allocated to PRAT Program

A total of $837,000 is currently allocated to the Pharmacology Research Associate Training (PRAT) Program for 1986. The PRAT Program budget will increase to $875,000 in 1987.

Mr. Stokes. Thank you, Mr. Chairman.

Mr. Natcher. Mr. Early.

RESEARCH CENTERS

Mr. Early. I want to go over something we have already gone over. On the request for centers, you are taking a 30 percent reduction in centers from 1985. You will go from 16 to 11?

Dr. Kirschstein. That is basically correct. The NIGMS supported 15 research center grants in 1985. The 1986 appropriation provided for 16 research centers. We now plan to fund 15 under the sequestration provisions in 1986, and the President's 1987 budget provides for 11 Centers.

Mr. Early. Doctor, you told Mr. Conte, the types of centers. I can get from your justifications, which centers will be reduced. Are these being closed because there is no potential in the centers, or closed totally due to a lack of money?

Dr. Kirschstein. Mr. Early, some difficult decisions had to be made due to the fiscal constraints affecting the proposed 1987 budget.

Mr. Early. I know all of that.

Dr. Kirschstein. This decision was made primarily because of fiscal constraints.

Mr. Early. In your professional opinion, do you think that these centers are less exciting than the other centers?

Dr. Kirschstein. They are up for competing renewal in fiscal year 1987.

Mr. Early. Did I hear you say that Dr. John Burke up at Massachusetts General, the originator of this artificial skin, that his center is going to be closed?

Dr. **Kirschstein**. It is one of the research endeavors that we will not be able to continue as a research center grant.

Mr. **Early**. You are straining to defend this budget.

I want to see the independence the directors have always shown. You are closing a center—and you said that they were going from State I to Stage II. I got the impression that that was exciting. But we are closing it.

Doctor, in addition to reducing the number of centers, you also propose to reduce the direct costs of the other 11 centers by 13 percent.

Dr. **Kirschstein**. Yes, sir, that is correct.

Mr. **Early**. What effect will these reductions have on the centers, doctor?

Dr. **Kirschstein**. The research that will be done through these center grants will clearly slow down. Mr. Early, one thing I would like to add, is that the NIGMS is very cognizant of the need for the kind of research that is done under many of these research center grants. Therefore, if it is not possible to continue to fund these particular centers, we will make every effort to support the type of research previously done at these centers through the individual research grant mechanism.

Mr. **Early**. Doctor, have you received any letters or any calls from any of the grantees in the centers that are going to be closed?

Dr. **Kirschstein**. Not yet.

Mr. **Early**. You have not? I am going to try to find out what they say in their letters to you, because the American people are entitled to know.

IMPACT OF BUDGET REDUCTIONS

Doctor, the justifications state that NIGMS has at its main mission the discovery of new knowledge, theories and concepts that undergirds the diseases supported by NIH.

Isn't it going to be difficult to meet your mission in 1987 with this budget request?

Dr. **Kirschstein**. We will not be able to support as much research as we have in the past.

Mr. **Early**. Your pay line is going down. In 1985, you supported 41 percent of the approved science, and now you will reduce that from 41 to 30 percent. You cannot tell us what we are missing out on in the science that you are not going to fund, can you?

Dr. **Kirschstein**. No, I cannot.

Mr. **Early**. Will the 1987 budget allow you to undertake any new initiatives?

Dr. **Kirschstein**. It will allow us to continue some of the exciting work we have supported in the past, but clearly will slow it down.

Mr. **Early**. Will it allow you to undertake any brand new initiatives?

Dr. **Kirschstein**. I don't think so.

Mr. **Early**. I thought the answer would just be no.

Doctor, tell us will any significant new initiatives or opportunities that we have under way be slowed down?

Dr. **Kirschstein**. I think the area of gene mapping will go forward more slowly. There is also an area that we have not mentioned up to now, which is the study of developmental biology. The great unknown question is how an organism develops from a single cell to a full-blown organism containing all the original genes, yet with some of those genes only expressed in certain of the tissues and organs while others are not. We are just beginning to understand some parts of this process; how some genes switch on and off in various tissues at various times during development. Some research opportunities in this area will not be fully exploited during the next year.

Mr. EARLY. Supply for the record research initiatives under way that are being slowed down. I want a list, a brief description, and the funding requirements that would be necessary to keep them up.

If we slow down on gene mapping, I don't see where that is good judgment.

[The information follows:]

LIST OF ONGOING NIGMS-SUPPORTED INITIATIVES AFFECTED BY BUDGET REDUCTIONS

The Institute's so-called "Current Services" budget level for 1987—the amount it would take in 1987 to avoid any decrease in activities from the revised 1986 level—is $547.9 million, roughly $76.3 million more than the amount provided in the Institute's 1987 budget request.

The following NIGMS initiatives would receive less funding support under the President's 1987 budget than they will in 1986:

1. Gene Mapping - Over 3,000 genetic diseases are currently known to afflict mankind, many of which are very debilitating, cause mental retardation, or are fatal for their victims. A large number of these diseases, including Down's syndrome, muscular dystrophy, cystic fibrosis, and sickle cell disease, are known to be the result of a single flaw in one of the estimated 100,000 genes possessed by humans. Efforts are currently underway in genetics research laboratories throughout the nation (many of which are working with NIGMS support) to identify the precise location of the genetic flaw associated with each disease, with the goal of eventually developing effective methods of treatment.

Within the past few years, researchers have determined the approximate locations of the genes associated with Huntington's disease, cystic fibrosis, muscular dystrophy, and hemophilia. Great progress has also been made in determining the genetic basis for some forms of heart disease, as well as for breast, colon and skin cancer. It is also now believed that it is within the realm of possibility to discover the sites of the genes which predispose people to Alzheimer's disease, arthritis, diabetes, duodenal ulcers, schizophrenia, manic depression, and alcoholism. The pace of developments in this area is directly dependent upon the number of research teams being funded.

2. Gene Therapy - There are, at present, no real cures for any genetic diseases. Currently, however, a number of investigators are exploring the possibilities, admittedly complex and difficult, of either replacing or repairing defective genes to eliminate the disorders which they cause. Foreign genes already have been transplanted successfully into animals. For example, at least one form of dwarfism in mice has been cured, but this research involved a method not useful for human gene therapy. Current candidates for attempts to cure genetic disorders in humans include two rare diseases (adenosine deaminase deficiency [ADA] and Lesch-Nyhan disease), both of which cause severe mental retardation and early death. Much fundamental work remains to be done to determine how gene therapy can be successfully achieved in humans.

3. Developmental Biology - The normal development of an individual organism from a single cell to a fully formed adult is known to be regulated by signals from regulatory genes which turn other genes on and off at just the right moments over a period of time. Failures in timing can be disastrous. Investigators in the field of molecular genetics are currently working on a number of studies designed to determine how, where and when regulatory genes act, with an eye toward understanding, and perhaps preventing,

developmental disorders. Furthermore, these same regulatory switches may play a role in the development or control of cancer and other diseases, heightening the importance of this research. Opportunities in this area have been stimulated by recent discoveries.

4. Effect of Calcium and Calcium-Sensitive Proteins - The normal functioning of a cell is regulated by constant communications which occur both within a cell and between cells. When such communication fails havoc and disease can result. A current NIGMS initiative is to support studies to elucidate the exact role of calcium and calcium-sensitive proteins in the cellular communication process. One of the most important of these proteins is calmodulin (a cellular protein which relays signals delivered by calcium ions). Research on this topic is critical to the study of numerous diseases including hypertension, cancer, and disorders of the central nervous system.

5. Gap Junction Studies - Gap junctions are structures in cell membranes which serve as paths for communication signals between cells. They serve, for example, as the principal path for the flow of electrical current between heart cells, and are thus necessary for successful propagation of the electrical and contractile waves throughout the heart which permit it to pump blood through the body. Gap junctions are also important paths for cell to cell communication during development — carrying signals of an unknown nature during development. Research in this area is still relatively new, with many avenues of investigation waiting to be explored.

6. Artificial Enzyme Studies - Enzymes are proteins which serve to catalyze or "speed up" a host of naturally occurring biochemical processes in the body. Seeking to synthetically produce large quantities of medically important substances which are available in only minute quantities in nature, investigators are now attempting to develop artificial enzymes which can be "programmed" to speed up the production of desired substances such as essential amino acids.

7. Stereospecific Production of Safer, More Effective Drugs - Many drugs can and do occur in two configurations, with each configuration producing markedly different effects in the body. Indeed, one configuration might cure a disease, while the other may actually be dangerous to the patient. Scientists are now focusing their research on the development of efficient new procedures for the production of only the beneficial configuration of a variety of important, biologically active molecules, so as to provide safer and more effective drugs. Findings will be applied to the synthesis of alkaloids, steroids, and other significant biochemicals.

8. Biophysics - The NIGMS reorganized approximately one year ago to take better advantage of a multitude of research opportunities opening up in the field of biophysics following advances in research instrumentation. Improvements in X-ray crystallography and nuclear magnetic resonance, in particular, are now allowing scientists to gain dramatic new information regarding the relationships between the structure and function of proteins and other so-called macromolecules. Of particular interest are investigations into the

mechanisms by which proteins and nucleic acids (DNA and RNA) interact, since this is thought to be critical to the normal functioning of cellular processes.

9. Biomedical Research Instrumentation Development - Advances in biomedical research are closely linked to advances in the research tools available to investigators. The NIGMS is currently providing support for a limited number of studies designed to combine several existing technologies to develop new equipment with capabilities beyond those of any single existing technology by itself. Many opportunities exist in this area, and resulting technologies will undoubtedly help "drive" the future course of research across a host of basic genetic, molecular and cellular fields, just as they have in recent years.

10. Wound Healing Following Burn Injury - The NIGMS is currently providing support to researchers seeking to follow-up on recent discoveries regarding factors which affect the speed and effectiveness of wound healing following serious burn injuries. Research in this area has shown, for example, that the exposure of patients with severe burns to high levels of oxygen during the first 4 hours after infection greatly increases their ability to fight bacterial infection. Research in this area is important to efforts to reduce the number of fatalities (12,000) currently occurring in the United States each year from burn injuries.

Research Training

11. Medical Scientist Training Program (MSTP) - The MSTP provides funding support for individuals seeking to obtain the combined M.D.-Ph.D. degree. Designed to address a continued shortage in the nation's supply of physician-researchers, this program is providing support for 597 trainees in FY 1987, 52 fewer than the 649 trainees supported in FY 1986, and 128 fewer than the number of trainees (725) recommended by the National Academy of Sciences (NAS).

12. Minority Access to Research Careers (MARC) Program - The MARC Program is designed to increase career opportunities for minority group members in biomedical research. A recent report issued by the NAS noted the success of the Honors Undergraduate component of this program in producing graduates with an excellent success rate in terms of entering science-related careers. The President's FY 1987 budget will provide support for 395 MARC trainees, 83 fewer than the number of trainees supported in FY 1986 and 75 fewer than the number recommended by the NAS.

13. Predoctoral (Pre-Ph.D.) Research Training - The number of NRSA predoctoral awards made by NIH in the basic biomedical sciences has been reduced by 12% since 1980, placing the number of predoctoral trainees considerally below the level recommended by the NAS. Recently, the NAS suggested that the NIH predoctoral bioscience training program be enlarged from the 1984 level of 3,400 trainees to 3,750 in 1988, and then to 4,150 by 1990.

The NIGMS has traditionally supported two-thirds of the predoctoral research trainees receiving assistance from the NIH. In 1987, the NIGMS will provide support for 2,561 trainees at the predoctoral level, compared to 2,733 trainees in FY 1986.

RESEARCH ON G-PROTEINS

Mr. **Early**. You mentioned research on G-proteins which are expected to shed light on Alzheimers and Parkinson's disease. Will that be slowed down?

Dr. **Kirschstein**. Yes, sir.

GENE MARKER

Mr. **Early**. On that gene marker for CF, are we doing everything in this budget to get there as quickly as possible?

Dr. **Kirschstein**. Research on cystic fibrosis is supported by the National Institutes of Diabetes, Digestive and Kidney Diseases, and there is also a good deal of this research being supported by the Cystic Fibrosis Foundation. Research on three possible markers for CF is currently being supported through some of the small biotechnology companies and the Cystic Fibrosis Foundation. The involvement of our Institute in this area is in the development of new techniques to better identify such markers.

Mr. **Early**. I was encouraged with Dr. Bowen's testimony. He will be our first MD as a Secretary of Health and Human Services, and I hope he will lend a little more support for these priorities instead of always getting Mr. Natcher to put the money back in.

Your Institute deals with the basic stage of science.

Over 30 percent reductions in every area. I don't kow how you conclude with any autonomy, Doctor.

NOBEL PRIZE WINNER

One final thing which I mentioned before, it was delightful that Drs. Brown and Goldstein received those awards because they were funded by NIGMS years for how many years?

Dr. **Kirschstein**. The NIGMS supported Drs. Brown and Goldstein from 1972 to 1977 while they did basic studies. In 1977, having found the receptor for cholesterol and having begun to concentrate their efforts on the study of the role of cholesterol in heart disease, their work was transferred to the National Heart, Lung and Blood Institute. This is an example of what we expect to have happen with the work NIGMS supports, namely that it moves on to more targeted areas.

Mr. **Early**. That is where it is supposed to go, to find a cure. I want to congratulate you and thank you for your professional appearance before our committee, although I didn't think you were nearly as candid as I would have hoped you would be.

Mr. **Natcher**. Mr. Stokes.

Mr. **Stokes**. I have some questions I will submit for the record.

Mr. **Natcher**. Very well, Dr. Kirschstein, we want to thank you and your associates for appearing before our committee at this time in behalf of your budget request for fiscal year 1987.

This has been a good hearing and we appreciate it.

[The following questions were submitted for the record:]

MINORITY PROGRAM AND PERSONNEL ISSUES

Mr. Stokes. Do you establish goals for your senior administrators for addressing minority program and personnel issues? If not, why not?

Dr. Kirschstein. Every year, the performance plan developed for each of the senior administrators in NIGMS includes one element focusing on their performance with regard to achieving and implementing the Institute's affirmative action objectives. These objectives include promoting equal employment opportunity in making all personnel-related decisions, such as those involving recruitment and employee training, and the need to suggest--both to me and to the Executive Secretaries of initial review groups--the names of minority candidates for membership on the Institute's advisory and review committees.

A recent NIH-wide initiative bearing on minority program issues is of particular relevance to NIGMS because of our significant research training activities. Several months ago, NIH revised its guidelines for the administration of institutional National Research Service Awards (training grants) in order to promote broader and more systematic efforts to recruit minority trainees into these research training programs. As part of this effort, NIGMS staff members with responsibility for either the review or program administration of training grants will now include a statement regarding the efforts of applicants to recruit and train individuals from underrepresented minority groups in the summary statements which are prepared for training grant applications.

Mr. Stokes. How do you hold your senior officers accountable for meeting those goals?

Dr. Kirschstein. When I assess the performance of each of my senior staff each year, I review their performance with regard to the element dealing with affirmative action, along with the other elements in their plan. Their eligibility for certain monetary rewards, such as SES bonuses, merit pay increases, and cash awards, is contingent in part on their satisfactory performance with regard to this element. Because of the Institute's record in supporting the participation of minorities in biomedical research, as evidenced by the growth and success of the Minority Access to Research Careers (MARC) Program and the routine recruitment of talented minorities to the NIGMS staff, Institute personnel clearly understand the importance of working to achieve affirmative action goals.

Mr. Stokes. For the record, please supply the following information for SES, senior level administrative, and senior level professional positions in your institute: the current number of all such positions and the current number of these positions occupied by Blacks.

Dr. Kirschstein. The information requested follows:

Senior Level Positions in NIGMS Occupied by Blacks

	Black Employees	Total
SES	—	5
Senior Level Administrative	1	9
Senior Level Professional	5	30

WORK OF NOBEL PRIZE WINNERS

Mr. Early. I note that the winners of the 1985 Nobel Prize in Physiology or Medicine--Drs. Michael Brown and Joseph Goldstein— were grantees of the NIGMS. Would you please explain their work and its importance?

Dr. Kirschstein. The Nobel Prize was awarded to Drs. Brown and Goldstein in recognition both of their basic research on cholesterol metabolism, and of its implications for treating several diseases, including atherosclerosis and familial hypercholesterolemia. In the early years of their collaboration, Brown and Goldstein investigated cholesterol uptake in cell cultures in an effort to determine how the cholesterol molecules get from the circulatory system into the cell. They tracked the cholesterol molecules to cell membranes and found that they attached to specialized receptors clustered in coated "pits" on the surface. They saw that when the receptors had collected their quota of cholesterol molecules, the "pits" were pinched into the cell, forming vesicles. Enzyme activity inside the cholesterol-laden vesicles then freed the cholesterol from the receptors and released it into the cell as a nutrient. Finally, the receptors were recycled back to the cell surface when the cellular supply of cholesterol fell short of the required amount. This early work regarding cholesterol receptors by Drs. Brown and Goldstein led to their important investigations of the genetic basis of, and potential therapies for both atherosclerosis and familial hypercholesterolemia--the latter being a serious and often fatal genetic disorder tied to defects in these receptors.

There are two types of familial hypercholesterolemia, distinguished by whether only one or both of the patient's genes coding for the cholesterol receptors are defective. The work of Drs. Brown and Goldstein suggests that drugs may be effectively used to treat those with a single defective gene, while liver transplantation may be the therapy of choice for those with both defective genes. Furthermore, Brown and Goldstein's research on cholesterol metabolism points toward a productive avenue of research related to the factors which promote development of atherosclerosis. Since diets high in saturated fats and cholesterol suppress production of the cholesterol receptors, thus leaving more cholesterol to flow through or clog the blood stream, their elucidation of the role that genetics and other factors play in cholesterol metabolism may prove helpful in determining the critical causes of atherosclerosis.

EFFECT OF FUNDING FEWER COMPETING AWARDS

Mr. Early. Dr. Kirschstein, the NIGMS supported 987 new and competing awards in 1985. Your revised estimate for 1986 provides for only 810 new and competing awards (a reduction of 177 grants), and the President's 1987 budget would reduce this even further, to 689 awards. What is the overall effect of these reductions?

Dr. Kirschstein. The overall effect of these reductions in support for new and competing research project grant awards is a slowing down of the pace of biomedical research discoveries in those areas within the scope of the Institute's responsibility. In the area of genetics research, for example, the NIGMS will support 98 fewer new and competing awards in 1987 than it did in 1985; and similar decreases occur in the other NIGMS programs. This obviously means that only the highest priority research will be funded.

Mr. Early. Doctor, your FY 1987 budget request reflects a 20% reduction in the number of new and competing grants research grants when compared to FY 85 and FY 86. Is this substantial reduction of concern to you, Doctor?

Dr. Kirschstein. Yes, a reduction of this magnitude is of concern, both because of the number of research projects that must be delayed or abandoned and because of the signal that it sends to new investigators and those young people considering careers in biomedical research. I am confident, however, that a considerable amount of important progress will be made with the funds provided for research in the Institute's 1987 budget.

NEGOTIATED DIRECT COST REDUCTIONS

Mr. Early. For FY 87, the budget request proposes to reduce direct costs for noncompeting grants by 9.6% and for competing grants by 8.6%. Doctor, what do direct costs entail?

Dr. Kirschstein. Direct costs are those grant costs immediately and specifically associated with the conduct of a given research project, including the salaries of the principal investigator and his assistants, as well as expenses associated with the purchase and maintenance of essential laboratory equipment and the purchase of supplies.

Mr. Early. Doctor, what effect will these reductions have on research project grants?

Dr. Kirschstein. Reductions of this magnitude will require grantees to examine personnel and equipment needs, the areas where cost increases are most typical. This examination may result in their taking less expensive apporaches to their experiments--perhaps by employing fewer personnel and using older equipment. The purchase of supplies will also have to be cut back.

Mr. Early. Will the scope of projects be curtailed? Will research be delayed?

Dr. Kirschstein. In some cases, the scope of the projects may have to be curtailed. In almost all cases, the completion date of the research projects would be delayed.

Mr. Early. What effect will these reductions have on the quality of the research being conducted?

Dr. Kirschstein. The quality of the research being conducted would not necessarily be affected, although some aspects of particular projects would certainly be changed. It is the opinion of NIH staff, however, that direct cost reductions of greater than 10 percent could very well affect the viability of a research project.

GENETICS PROGRAM

Mr. Early. During these hearings, and in reviewing the budget request, it is apparent that progress in the field of genetics plays an important role in providing needed tools for research across the spectrum. Yet, in reviewing your budget request, I see that you are proposing over a 10% decrease in the area of genetic research. How do you justify this kind of decrease given the importance of this field to other areas of research?

Dr. Kirschstein. The availability of research tools previously developed in genetics research laboratories has opened up a host of exciting new research opportunities in other areas of biomedical research, including almost all the areas within the scope of the Institute's other research programs: cellular and molecular biology, biophysics, biochemistry, and pharmacology. Given the limited budgetary resources available in 1987, the NIGMS found it necessary to reduce the proportion of its total research budget allocated to the Genetics Program in order to explore as many of these other research opportunities as funds will permit. Despite this, the allocation to the Genetics Program will still be approximately one-third of the Institute's total budget--a strong indication of the continued importance of research studies concerned with the fundamental mechanisms of inheritance.

RESEARCH ADVANCES IN GENETICS

Mr. Early. What kinds of research advances are on the horizon with regard to genetic disease?

Dr. Kirschstein. There are several categories of research advances on the horizon that will improve our ability to deal with genetic disorders. In the near-term, analysis of DNA by restriction fragment length polymorphisms (RFLPs), about which you have heard, will permit the early detection of many diseases, even when the underlying genetic defect is not yet known. This methodology is already being used to study individuals at risk for hemophilia, the thalassemias, sickle cell anemia, and one form of muscular dystrophy. It is also being used experimentally to detect Huntington's disease, cystic fibrosis, and polycystic kidney disease. Since many other devastating genetic disorders are also amenable to this sort of detection, it is only a matter of time before informative RFLP's are identified to make detection possible. Currently under investigation are RFLPs for Tourette's syndrome, ocular albinism, mucopolysaccharide storage diseases, tuberous sclerosis, neurofibromatosis, and bipolar depressive disease.

Recently, the gene that causes familial hypercholesterolemia was located, and it will eventually be feasible to screen individuals for mutations in this gene, which can lead to abnormally high blood cholesterol levels and myocardial infarctions. Detected early, individuals with hypercholesterolemia can modify their diets or be treated with drugs to reduce their cholesterol levels.

Genetic research has also led to a better understanding of certain kinds of cancer. Within the last 4 years, scientists have discovered that specific chromosomal abnormalities are associated with particular cancers, including leukemias, lymphomas, and carcinomas. These chromosomal abnormalities are important in early diagnosis and also open avenues for investigating the causes of these cancers.

Recent breakthroughs in genetic research also hold promise farther into the future. Recombinant DNA technology will allow identification of normal gene products whose expression is disrupted in genetic diseases. This will permit development of more rational therapies to treat these diseases. In addition, research on gene expression, DNA recombination, and chromosomal structure should improve prospects for replacing defective genes in patients with certain types of diseases.

Eventually, a basic understanding of genetics is likely to have an impact on attempts to prevent developmental defects. Although 2-3% of all infants are born with major malformations, little is known about the genes that are involved. Animal models, particularly fruit flies and roundworms, are opening up new areas of research which suggest roles for a highly complex hierarchy of genes responsible for regulating development.

MEDICAL SCIENTIST TRAINING PROGRAM

Mr. Early. What will be the effect of the President's FY 1987 budget on the Medical Scientist Training Program, which is administered by your institute?

Dr. Kirschstein. The President's 1987 budget will provide support for 597 individuals seeking the combined M.D.-Ph.D. degree. This is 52 fewer trainees than the number to be supported in 1986, and 128 fewer than the number of trainees (725) recommended by the National Academy of Sciences.

RESEARCH CENTERS SUPPORT IN 1986

Mr. Early. Doctor, in looking at your budget request, I see that you will fund 15 research centers rather than the 16 originally contemplated. What type of center will you have to forego and what effect will this have on your research programs?

Dr. Kirschstein. The NIGMS will support three research center grants in genetics in 1986, rather than the four originally projected. While some collaborative work on genetic diseases between basic research scientists and clinical investigators will no longer be supported through this center grant, some of the participating investigators may receive grant support through individual research projects, thus continuing their work.

Mr. Early. Will there be downward negotiations in research centers in FY 86 and, if so, to what extent?

Dr. Kirschstein. The Institute's revised budget for 1986 assumes only a very small downward negotiation in direct costs for research center grants, approximately one percent.

RESEARCH CENTERS SUPPORT IN 1987

Mr. Early. In reviewing your FY 87 request, I see that you are proposing to eliminate four research centers. What types of centers will be eliminated and why are you proposing their elimination?

Dr. Kirschstein. Of the four research center grants to be eliminated in 1987, two are concerned with trauma and burn research, one with pharmacology research and one with genetics research.

Mr. Early. What effect will the elimination of these centers have on the Institute's research program? Is the type of research being conducted at these centers the same as that of the remaining centers?

Dr. Kirschstein. The NIGMS utilizes the research center grant mechanism to encourage interaction and cooperation between basic laboratory researchers and clinical investigators, either because such interaction requires some encouragement or because it is vital to dealing with a certain kind of research problem--determining the best approaches for the treatment of severe burn injuries, for example. The elimination of four research center grants will necessarily reduce the opportunities available for such collaboration in 1987.

Within each research category--burn and trauma research, for example--the kinds of research being conducted are similar in scope from center to center, although different aspects of a problem may be emphasized and different approaches are likely to be used.

Mr. Early. Would you please provide a list of the research centers currently funded and indicate which ones will be up for renewal in FY 1987.

Dr. Kirschstein. The information requested is as follows:

NIGMS Research Center Grants Funded in 1985
(Dollars in Thousands)

Pharmacological Sciences		
1.	Vanderbilt University (Dr. Oates)	-- $687
2.	State University of New York at Buffalo (Dr. Levy)	— 447
3.	University of California, San Francisco (Dr. Benet)	— 314 2/
Anesthesiology		
4.	Massachusetts General Hospital (Dr. Kitz)	— 680
Trauma and Burn Research		
--	Albany Medical College (Dr. Shah)	— 68*
5.	University of Texas (Dr. Baxter)	— 354
6.	Massachusetts General Hospital (Dr. Burke)	— 596
7.	University of Washington (Dr. Carrico)	— 527
8.	Cornell University (Dr. Shires)	— 391 2/
9.	University of California, San Francisco (Dr. Hunt)	— 431 2/
10.	Brigham and Women's Hospital, Boston (Dr. Wilmore)	-- 818
Genetics		
11.	University of Washington (Dr. Motulsky)	-- 801 2/
12.	University of California, San Diego (Dr. Seegmiller)	-- 730 1/
13.	Yale University (Dr. Ward)	— 844
14.	University of Pennsylvania (Dr. Schmickel)	-- 784
Molecular Pathology		
15.	Yale University (Dr. Palade)	-- 763
	Total	9,235

* Received supplement only in 1985
1/ Up for Renewal in 1986
2/ Up for Renewal in 1987

EFFECT OF CENTER GRANT REDUCTIONS

Mr. Early. Doctor, will you summarize with some specificity, the effect the proposed reductions in the number, size and scope of the centers program will have on the institute's program plans--both immediate and long-range?

Dr. Kirschstein. The kind of basic research supported by the NIGMS is best supported through the use of the individual, investigator-initiated research project grant mechanism. We do believe, however, that in some areas it is appropriate--when the scientific conditions are right--to encourage collaboration between clinical and laboratory investigators; and this is best done through research center grants. The proposed reduction in center grant support in 1987 would have the effect of delaying some efforts along these lines in such areas as trauma and burn research and medical genetics.

Over the past few years, the number of research center grants supported by the NIGMS has been reduced, and this has had an effect on the Institute's ability to bring clinical researchers together with laboratory scientists as much as we would like. Our plans--both immediate and long-range--call for the use of the research project grant mechanism to support some of the kinds of research previously supported through center grants.

OTHER RESEARCH

Mr. Early. Doctor, in reviewing your budget request, I see that you are proposing a substantial decrease in FY 87 in the area of "other research" with the number of awards dropping from 28 in FY 85 to 2 in FY 87. What kinds of activities were supported in FY 85? And, what activities will be supported in FY 86?

Dr. Kirschstein. The "Other Research" category includes funds for a variety of activities related to the Institute's overall mission of supporting biomedical research. These include research career awards, research career development awards, scientific conferences and scientific review evalution awards (SREAs)--the latter being a mechanism for the support of the NIH peer review system. Within the category of "Other Research," there is a sub-category, simply called "Other," which includes funds for both SREAs and scientific conferences. This sub-category has been reduced from 24 awards in 1985 to only 2 awards in 1987, with all of the eliminated awards representing scientific conferences.

Mr. Early. Why are you proposing to virtually eliminate activities in this category?

Dr. Kirschstein. Given the limitation on funds made available to the NIGMS within the President's 1987 budget, it was necessary for the Institute to reduce its support for research conference grants.

Mr. Early. What impact will termination of activities in this category have on your research program?

Dr. Kirschstein. The impact will be minimal if the organizers of these scientific conferences are able to obtain support from other sources. To the extent that conferences are cancelled, however, or that fewer researchers are able to attend such conferences, the communication of research findings within the scientific community will be hindered.

POTENTIAL NEW RESEARCH INITIATIVES

Mr. Early. Will any significant new research initiatives or opportunities be lost or delayed by lack of funds in the FY 87 budget?

Dr. Kirschstein. The NIGMS research budget for 1987 includes funds for 689 new and competing research project grants--15 percent fewer than the number to be awarded in 1986 (810). This reduction will eliminate the possibility of starting any major new research initiatives next year, although opportunities do exist.

Mr. Early. Please provide, for the record, a list of these along with a brief description and the funding requirements associated with each.

Dr. Kirschstein. The information requested follows. The total cost involved would be $50 million.

LIST OF POTENTIAL NEW INITIATIVES

1. Medical Genetics - Geneticists have recently undertaken a new approach in their attempts to develop effective methods for the early diagnosis of genetic diseases, studying genes obtained from entire extended families where some members are known victims of specific disorders (e.g., Huntington's disease), in order to identify the specific nucleotide sequence (genetic code) which causes the disease. This method has been successfully applied in the prenatal diagnosis of various thalassemias, as well as sickle cell disease, and is now potentially available for the prenatal diagnosis of PKU, X-linked retinitis pigmentosa and Huntington's disease. Future advances in this area will depend upon the progress of investigators, using a method called "chromosome walking," in detecting the specific DNA changes which occur in given diseases. When the exact location and nature of the DNA mutations are established, the diagnoses of genetic diseases may be possible by the use of these more direct methodologies.

2. Genetic Analysis of Mitosis - Mitosis, the distribution of a complete set of chromosomes containing genetic material to each daughter cell prior to cell division, is a complex process. It usually occurs with a high degree of fidelity, but when a cell fails to transmit correctly one of the complement of chromosomes the effect on the organism is serious. Studies conducted primarily in yeast cells have led to a better understanding of the molecular details of mitosis. In the past year, several technological and conceptual advances have allowed scientists to characterize many

components of the mitotic apparatus that were previously inaccessible to study. Continued work in the area should lead to a better understanding of normal chromosomal behavior and of the causes of abnormal distribution of chromosomes that lead to various developmental defects in humans.

3. Pharmacology of Immunosuppressant Drugs - The liver is a major site for the metabolism (breakdown) of many drugs and biochemicals, allowing these substances to be made water-soluble for elimination from the body. In patients undergoing immunosuppressive therapy following liver transplantation, it is especially important to know the metabolic status of the immunosuppressant drugs used, as well as any other drugs to which the patient might be exposed. The NIGMS' Pharmacological Sciences Program is currently interested in supporting a research initiative in this area, with a focus on the genetic determinants of the metabolism of immunosuppressant drugs by different individuals.

4. Studies of Specific Protease Inhibitors - Proteases are enzymes known to catalyze or speed-up the breakdown of biologically active molecules, such as proteins and peptides, which are critical to the regulation of the nervous and immune systems, as well as in the control of blood pressure, cell growth, and digestion. If a group of proteases do not function properly, certain disease states can result; e.g., heart failure, psychiatric disorders, digestive ailments, and high blood pressure.

To more clearly understand the origin of such disorders, the Pharmacological Sciences Program is seeking to identify substances which can selectively inhibit, or turn off, certain proteases so that the effects can be observed. Research in this area has important implications for the study of many diseases.

5. DNA Studies - An NIGMS grantee recently has developed an important new technique to analyze larger segments of DNA than was previously possible. A variation of "gel electrophoresis," the technique involved offers the first opportunity for analyzing whole chromosomes of organisms such as parasites, algae and fungi, and has already been used to study trypanosomes, a species of which causes sleeping sickness. Studies in this area have already yielded information related to the mechanism by which trypanosomes evade the body's immune system. With further support, research in this area is expected to eventually allow investigators to study the intact chromosomes of fruit flies, mice, and even humans.

6. Biotechnology in the Study of Receptor Structure and Function - The new biotechnology now available for the sequence analysis of proteins and nucleic acids, coupled with advanced methods for separating constituents, is setting the stage for progress in discovering the detailed structure and function of cellular receptors. Receptors are molecules or constellations of molecules that are characterized on the one hand by their ability to recognize circulating substances in blood and other body fluids (e.g., hormones) and on the other hand by the characteristic response of the cell to the substances that they mediate. Cellular receptors play essential roles in immune responses and in the actions of hormones and neurotransmitters.

7. Mechanistic Enzymology - Researchers involved in biochemical and biophysical studies of enzymes, the biological catalysts, are gaining growing sophistication in describing and explaining how enzymes work. This is of great importance to not only an understanding of most functions of the human body, but to aspects of agriculture and the production of substances important in the treatment of disease as well.

8. Spectroscopic NMR Imaging of Sodium and Protons - Biophysics researchers are increasingly finding new ways to use nuclear magnetic resonance (NMR) imaging in a number of important biomedical research areas. One new initiative, for example, involves an exciting effort to create images of sodium ions in the body to provide information not readily available from other techniques, information which may be useful in the detection of strokes, tumors and other abnormalities. The NMR imaging of protons is also being explored; and while the clinical value of proton imaging cannot yet be estimated, it is likely that it will provide the ability to detect areas of local ischemia (lack of blood), an ability that could have important clinical uses. Applications of proton imaging to heart and tumor studies are considered particularly promising. Research on these topics is just beginning.

9. Biochemical Transport Studies - Many biological processes depend upon the successful transportation of biochemicals and nutrients into or out of cells. An NIGMS grantee has recently developed new genetic and immunological tools for examining the mechanisms by which glucose is transported into cells, and his success has opened up exciting research opportunities related to a host of diseases where either too much or too little of a substance tends to be transported, including many types of diabetes, in which cellular glucose transport is defective.

USE OF ADDITIONAL FUNDS

Mr. Early. If an increase over the FY 87 request is provided, how would you use these additional funds?

Dr. Kirschstein. In priority order, any additional funds provided to the NIGMS in 1987 would be used to: (1) Bring support for direct research costs on research grant awards up to historical levels; (2) Support additional competing research project grants, especially in the areas of genetics and molecular biology research; (3) Provide support for additional pre and postdoctoral research trainees, including additional support for trainees supported through the MARC and Medical Scientist Training Programs; and (4) Increase support for research center grant awards.

G-PROTEINS

Mr. Early. In your justification materials, you mention research on "G-proteins," which is expected to shed light on studies of cancer formation, Alzheimer's disease, Parkinson's disease, as well as other disorders. Would you please elaborate on this for us.

Dr. Kirschstein. Research suggests that the family of so-called "G-proteins" plays an important role in various cellular processes that involve transfer of chemical signals, such as hormones and neurotransmitters, from outside the cell, into information vital to cellular activity. Since both Alzheimer's disease and Parkinson's disease are believed to be disorders related to malfunctioning neurotransmission, some scientists are investigating whether defects in the G-protein (or its precursor gene) may be involved in the faulty signalling characteristic of these debilitating diseases. Should this prove true, it might be possible to determine if a person is at risk for these disorders, as it is now possible to detect a tendency to develop pseudohypoparathyroidism, a disease known to be caused by a genetic deficit in a certain G-protein.

One class of G-proteins is the ras proteins, which are found in yeast and mammals and, in the latter, are the product of the ras oncogene (a gene related to cancer formation). Studies in yeast demonstrate that activation of their G-ras proteins triggers proliferation. Since cancer is also characterized by abnormal cell proliferation, and the mammalian equivalent of the yeast's G-ras protein is already known to be produced by an oncogene, scientists feel that the cancer process might be elucidated by improving our understanding of how this particular G-protein is activated, and how it differs from other G-proteins.

DEVELOPMENT OF ARTIFICIAL ENZYMES

Mr. Early. Would you bring us up to date on the progress that has been made in developing artificial enzymes?

Dr. Kirschstein. Enzymes are proteins that speed up or catalyze biological reactions. Investigators are now able to produce artificial enzymes having catalytic rates approaching those achieved by natural enzymes. The design and synthesis of artificial enzymes enables scientists to produce models of that portion of the enzyme which catalyzes the reaction and to identify the specific function of each portion of this catalytic site. Furthermore, it is becoming possible to produce artificial enzymes that have binding specificities that are different from those of natural enzymes. This will enable scientists to tailor-make reactions by substituting new molecules for the ones that normally participate. A current example is the development of an artificial enzyme that catalyzes the synthesis of tryptophan, an amino acid that is an essential dietary component for humans. The potential usefulness of artificial enzymes includes the structurally specific and efficient production of previously scarce substances, or new substances, including drugs. When fully developed, artificial enzymes hold the potential of being important industrial tools for the pharmaceutical, agricultural, biomaterials and chemical industries.

Mr. Early. If successful, what implications does this have for the prevention, treatment and cure of diseases?

Dr. Kirschstein. Possible implications of the development of artificial enzymes for the prevention, treatment, and cure of disease, in addition to the development of new pharmaceutical agents, include: (1) the development of an artificial enzyme model to facilitate understanding of the functions of natural enzymes and the modification of such a model to mimic abnormal enzyme functions characteristic of certain disease states; and (2) the possibility, far in the future, of using artificial enzymes as therapeutic agents for patients genetically deficient in particular enzymic activities.

PHARMACOLOGICAL SCIENCES RESEARCH

Mr. Early. Have we made any progress in the area of pharmacological sciences within the past year? Would you highlight some of the major advances in this area and briefly explain their importance to other areas of research.

Dr. Kirschstein. Within the past year, a number of major advances achieved by grantees of the Pharmacological Sciences Program have occurred; among them are the following:

1. Scientists have discovered a number of factors that influence how individuals respond to the corticosteroid class of drugs, one of the most commonly prescribed to treat arthritis, asthma, skin disorders and shock, and to prevent host-tissue rejection following organ transplantation. Because numerous antibiotics, most oral contraceptives, and certain anti-convulsive drugs affect the rate of metabolism of corticosteroids, and because some tissues trap these steroids, thus preventing them from exerting their full therapeutic effect at their target sites, proper individualized dosages must be determined by taking all of these factors into consideration.

2. Many important biological molecules, including therapeutic drugs, can exist in two configurations which are mirror images of each other, such as the right and left hands are mirror images. As a general rule, only one of the configurations has biological activity. The other configuration may be inactive or may actually interfere with the activity of the desired configuration. In some cases, one of the mirror molecular configurations of a drug may even be responsible for undesirable side effects. Most traditional methods of synthesizing these important therapeutic molecules have resulted in mixtures of the two configurations. However, Dr. Herbert Brown has recently adapted the process of hydroboration, for which he was awarded the Nobel Prize for Chemistry in 1979, to synthesize only the active and safer configuration of drugs.

3. Scientists have elucidated the structural properties and the binding sites of proteins of the acetylcholine neurotransmitter system, a vital intercellular communication system, defects in which are implicated in Alzheimer's disease and myasthenia gravis. Research results include identification of the receptor sites at which this neurotransmitter binds, and determinations of the geometry of the receptor sites and the distance between them. This work is being applied to research into how drugs might be better designed to treat pathologic conditions involving these receptors. This same research has provided useful insights for physiologists studying the channels for sodium in cells and for enzymologists as well.

4. As previously mentioned, research concerned with G-proteins is burgeoning. One important study of G-proteins has led to the discovery that cells that do not respond to a stimulus resulting from G-protein activation do not have messenger RNA for the G-protein. If a clone for the G-protein gene is inserted into these

cells, they proceed to make messenger RNA and the G-protein, and to function normally in response to a stimulus. Since these G-proteins play important roles in fundamental life processes, including neurotransmission, protein synthesis, immunological responses, vision and cell proliferation, these findings can be expected to have a major impact in cancer research, immunology, biochemistry, endocrinology, and neurobiology.

LASER TECHNOLOGY

Mr. Early. What progress has been made in the area of lasers?

Dr. Kirschstein. The development of laser technology has had a major impact on programs funded by NIGMS. An extremely important feature is the ability of lasers to provide intense light for extremely short periods of time—on the order of picoseconds. (For comparison purposes, the relationship between a picosecond and a second is the same as between one second and 10,000 years). The use of these pulsed lasers has made it possible to examine movement inside protein and nucleic acid molecules at their most fundamental level. In addition, the use of lasers is providing basic information on how oxygen binds to the oxygen transport protein hemoglobin, how light is transformed into nerve impulses in vision, and how energy is transferred at the cellular level.

An important feature of this research is that the scientists who are involved in the application of lasers to biological systems have also been involved in advancing laser technology itself, particularly in adapting it to be better utilized in biomedical research. This has evolved so that today there is a close working relationship between these scientists and the laser industry itself.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

National Institute of General Medical Sciences

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NATIONAL INSTITUTES OF HEALTH

National Institute of General Medical Sciences

For carrying out section 301 and title IV of the Public Health Service Act with respect to general medical sciences, [$514,814,000] *$471,533,000. (Department of Health and Human Services Appropriation Act, 1986).*

NATIONAL INSTITUTES OF HEALTH

National Institute of General Medical Sciences

Amounts Available for Obligation 1/

	1985	1986	1987
Appropriation	$482,260,000	$514,814,000	$471,533,000
Enacted administrative reduction	---	-49,000	---
Sequester order	---	-22,135,000	---
Proposed rescission	---	-7,358,000	---
Subtotal, adjusted appropriation	482,260,000	485,272,000	471,533,000
Comparative transfer for changes in the Central Services financing mechanisms and formulas from:			
National Institute Environmental Health Sciences	+49,000	---	---
Fogarty International Center	+41,000	---	---
Office of Director	+374,000	---	---
National Institute of Mental Health	+185,000	---	---
Total	+649,000	---	---
Subtotal, adjusted budget authority	482,909,000	485,272,000	471,533,000
Unobligated balance, start of year	---	+1,171,000	---
Unobligated balance, end of year	-1,171,000	---	---
Unobligated balance, lapsing	-114,000	-237,000	---
Total obligations	481,624,000	486,206,000	471,533,000

1/ Excludes the following amounts for reimbursable activities carried out by this account: 1985 -- $217,000; 1986 -- $1,715,000; 1987 -- $300,000.

NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES

Budget Mechanism

(Dollars In Thousands)

	1986 Appropriation 1/		1986 Available after Sequestering 1/ 2/		1986 Revised Estimate 1/ 2/		1987	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research grants:								
Research projects								
Noncompeting............	1,971	$290,228	1,971	$277,748	1,971	$278,918	2,082	$292,509
Admin. supplemental......	(17)	675	(17)	646	(17)	633	(17)	703
Competing								
Renewal................	507	84,630	507	83,539	435	77,753	343	59,357
New....................	452	53,057	452	48,265	363	45,582	338	40,821
Supplemental...........	13	1,105	13	1,070	12	1,024	8	689
Subtotal, competing..	972	138,792	972	132,874	810	124,359	689	100,867
Subtotal, research projects.........	2,943	429,695	2,943	411,268	2,781	403,910	2,771	394,079
Research Centers								
Pharmacological sciences.	3	1,669	3	1,669	3	1,669	2	1,151
Anesthesiology...........	1	671	1	671	1	671	1	584
Trauma and burn..........	8	4,177	7	3,738	7	3,738	5	2,404
Genetic..................	3	2,784	3	2,784	3	2,784	2	1,621
Molecular pathology......	1	918	1	918	1	918	1	799
Subtotal res. ctrs.....	16	10,219	15	9,780	15	9,780	11	6,559
Other research								
Research career program..	16	611	15	585	15	585	18	677
Other....................	21	2,253	17	1,920	17	1,920	2	1,865
Subtotal, other res....	37	2,864	32	2,505	32	2,505	20	2,542
Total, research grants.......	2,996	442,778	2,990	423,553	2,828	416,195	2,802	403,180

Training:								
Individual awards								
Noncompeting.............	275	6,045	275	6,045	275	6,045	194	4,484
Competing, new...........	70	1,633	37	786	37	786		
Subtotal, individ......	345	7,678	312	6,831	312	6,831	194	4,484
Institutional awards								
Noncompeting.............	2,725	47,128	2,725	47,128	2,725	47,128	2,603	48,432
Competing, renewal.......	169	2,915	71	1,280	71	1,280		
Subtotal, inst.......	2,894	50,043	2,796	48,408	2,796	48,408	2,603	48,432
Total, training............	3,239	57,721	3,108	55,239	3,108	55,239	2,797	52,916
Research and development contracts..................	5	1,263	5	1,209	5	1,209	5	1,263
Intramural research..........		875		837	FTE 21	837	FTE 21	875
Researach management and support....................		13,299		12,726	139	12,726	139	13,299
TOTAL......................		515,936		493,564	160	486,206	160	471,533

1/ Reflects an enacted administrative reduction of $49,000 and a carryover in unobligated funds of $1,171,000.

2/ Reflects a consultant services (Section 515 of the Treasury-Postal Service Appropriation Act, 1985) withholding of $237,000.

NATIONAL INSTITUTES OF HEALTH

National Institute of General Medical Sciences

CROSSWALK -1986 Appropriation
(Dollars in thousands)

MECHANISM

PROGRAM ACTIVITY	Research Grants			Training Programs		Res. & Develop. Contracts	Intra-mural Research	Research Management and Support	Total
	Research Projects	Research Centers	Other Research	Individual	Institutional				
Cellular and molecular basis of disease...........	$123,617	$918	$240	$1,744	$20,272	$65			$146,856
Genetics......................	161,671	2,784	364	4,084	1,226	1,198			171,327
Pharmacological sciences.....	66,235	2,340	286	555	4,950	0			74,366
Biophysics and physiological sciences..................	78,172	4,177	1,974	194	16,746	0			101,263
Minority access to research careers....................				1,101	6,849				7,950
Intramural research.........							$875		875
Research mgmt. and support..								$13,299	13,299
Total.......................	429,695	10,219	2,864	7,678	50,043	1,263	875	13,299	515,936

NATIONAL INSTITUTES OF HEALTH

National Institute of General Medical Sciences

CROSSWALK -1986 Available After Sequestering
(Dollars in thousands)

PROGRAM ACTIVITY	MECHANISM								
	Research Grants			Training Programs		Res. & Develop. Contracts	Intra-mural Research	Research Management and Support	Total
	Research Projects	Research Centers	Other Research	Individual	Institutional				
Cellular and molecular basis of disease............	$118,277	$918	$192	$1,494	$19,527	$65			$140,473
Genetics......................	155,294	2,784	315	3,591	1,226	1,144			164,354
Pharmacological sciences.....	63,153	2,340	286	478	4,800	0			71,057
Biophysics and physiological sciences..................	74,544	3,738	1,712	167	16,006	0			96,167
Minority access to research careers..................				1,101	6,849				7,950
Intramural research..........							$837		837
Research mgmt. and support..								$12,726	12,726
Total.......................	411,268	9,780	2,505	6,831	48,408	1,209	837	12,726	493,564

NATIONAL INSTITUTES OF HEALTH

National Institute of General Medical Sciences

CROSSWALK -1986 Revised Estimate
(Dollars in thousands)

PROGRAM ACTIVITY	MECHANISM								
	Research Grants			Training Programs		Res. & Develop. Contracts	Intra-mural Research	Research Management and Support	Total
	Research Projects	Research Centers	Other Research	Individual	Institutional				
Cellular and molecular basis of disease...........	$116,017	$918	$192	$1,494	$19,527	$65			$138,213
Genetics......................	152,592	2,784	315	3,591	1,226	1,144			161,652
Pharmacological sciences.....	62,054	2,340	286	478	4,800	0			69,958
Biophysics and physiological sciences..................	73,247	3,738	1,712	167	16,006	0			94,870
Minority access to research careers....................				1,101	6,849				7,950
Intramural research.........							$837		837
Research mgmt. and support..								$12,726	12,726
Total........................	403,910	9,780	2,505	6,831	48,408	1,209	837	12,726	486,206

NATIONAL INSTITUTES OF HEALTH

National Institute of General Medical Sciences

CROSSWALK -1987 Congressional Justification
(Dollars in thousands)

	MECHANISM								
	Research Grants			Training Programs					
PROGRAM ACTIVITY	Research Projects	Research Centers	Other Research	Individual	Institutional	Res. & Develop. Contracts	Intra-mural Research	Research Management and Support	Total
Cellular and molecular basis of disease...........	$113,815	$799	$182	$821	$20,770	$65			$136,452
Genetics......................	143,317	1,621	254	2,029	501	1,198			148,920
Pharmacological sciences.....	63,000	1,735	160	585	4,667	0			70,147
Biophysics and physiological sciences..................	73,947	2,404	1,946	115	16,362	0			94,774
Minority access to research careers....................				934	6,132				7,066
Intramural research.........							$875		875
Research mgmt. and support..								$13,299	13,299
Total.......................	394,079	6,559	2,542	4,484	48,432	1,263	875	13,299	471,533

National Institute of General Medical Sciences

Summary of Changes

1986 Current estimated Obligations..............................	$486,206,000
1987 Estimated Obligations......................................	471,533,000
Net change..	-14,673,000

	1986 Base	Change from Base
Increases:		
A. Built-in:		
1. Within-grade pay increase.....	$5,704,000	+$62,000
2. Federal Employee Compensation Fund increase..............	30,000	+5,000
3. FTS Rate Increase..............	84,000	+23,000
4. Service and supply fund increase................	1,143,000	+48,000
5. Increased costs of supplies, materials and other expenses	6,200,000	+144,000
Subtotal.........		+282,000
B. Program:		
1. Research projects:		
a. Noncompeting continuations converting from competing status....................	279,551,000	+105,575,000
b. Competing (new, renewals and supplementals)........	124,359,000	+100,867,000
2. Research centers:		
a. Noncompeting continuations converting from competing status....................	6,606,000	+1,278,000
b. Competing (new and renewals)................	3,174,000	+387,000

Summary of Changes - continued

	1986 Base	Change from Base
3. Other research:		
a. Noncompeting continuations converting from competing status....................	2,010,000	+409,000
b. Competing (new and renewals..................	495,000	+123,000
4. Individual training awards:		
a. Noncompeting continuations converting from competing status....................	6,045,000	+1,022,000
b. Competing (new and renewals).................	786,000	---
5. Institutional training awards:		
a. Noncompeting continuations converting from competing status....................	47,128,000	+3,866,000
b. Competing (new and renewals).................	1,280,000	---
6. Research and development contracts....................		
a. Continuations	1,209,000	+54,000
7. Intramural research: Increase in high priority areas.............	837,000	+26,000
8. Research management and support: Increase in high priority areas.............	12,726,000	+683,000
Subtotal............		+214,290,000
Total increases...		+214,572,000

Decreases:

A. Built-in:

	1986 Base	Change from Base
1. Decrease in payment for centrally furnished services	4,616,000	-380,000
Subtotal.................		-380,000

Summary of Changes - continued

	1986 Base	Change from Base
B. Program:		
1. Research projects:		
a. Noncompeting completed or converting to competing status....................	279,551,000	-91,914,000
b. Competing completed or converting to noncompeting status.........	124,359,000	-124,359,000
2. Research centers:		
a. Noncompeting completed or converting to competing status....................	6,606,000	-1,712,000
b. Competing completed or converting to noncompeting status....................	3,174,000	-3,174,000
3. Other research:		
a. Noncompeting completed or converting to competing status....................	2,010,000	—
b. Competing completed or converting to noncompeting status....................	495,000	-495,000
4. Individual training awards:		
a. Noncompeting completed or converting to competing status....................	6,045,000	-2,583,000
b. Competing completed or converting to noncompeting status....................	786,000	-786,000
5. Institutional training awards:		
a. Noncompeting completed or converting to competing status....................	47,128,000	-2,562,000
b. Competing completed or converting to noncompeting status....................	1,280,000	-1,280,000
Subtotal, program.........		-228,865,000
Total, decrease...............		-229,245,000
Total, net change.....................		-14,673,000

National Institute of General Medical Sciences

Budget Authority by Activity

(Dollars in thousands)

	1986 Appropriation	1986 Available after Sequestering	1986 Revised		1987 Estimate	
	Amount	Amount	FTE	Amount	FTE	Amount
Cellular and molecular basis of disease.......	$146,856	$140,473	---	$138,213	---	$136,452
Genetics......	171,327	164,354	---	161,652	---	148,920
Pharmacological sciences......	74,366	71,057	---	69,958	---	70,147
Biophysics and Physiological Sciences......	101,263	96,167	---	94,870	---	94,774
Minority access to research careers.......	7,950	7,950	---	7,950	---	7,066
Intramural research......	875	837	21	837	21	875
Research Management and Support.......	13,299	12,726	139	12,726	139	13,299
Total Obligations.	515,936	493,564	160	486,206	160	471,533
Unobligated balance, start of year........	-1,171	-1,171		-1,171		
Unobligated balance lapsing.......	---	237	---	237	---	---
Total budget authority.....	514,765	492,630	160	485,272	160	471,533

Note: All 1986 columns reflect an enacted administrative reduction of $49.000.

National Institute of General Medical Sciences

Obligations by Object

	1985 Actual	1986 Revised Estimate	1987 Estimate
Total number of full-time permanent positions................	165	165	165
Total compensable work years: Full-time equivalent employment....	162	161	161
Average ES salary.....................	66,232	62,920	62,920
Average GS grade......................	9.14	9.14	9.14
Average GS salary.....................	28,224	26,813	26,813
Average salary, grades established by act of July 1, 1944 (42 U.S.C. 207)	35,361	33,593	33,593
Average salary of ungraded positions.	23,206	22,046	22,046
Personnel compensation:			
Permanent positions................	4,301	4,313	4,516
Positions other than permanent.....	662	666	695
Other personnel compensation.......	77	78	81
Subtotal, personnel compensation.	5,040	5,057	5,292
Personnel benefits..................	627	636	658
Benefits for former personnel........	11	11	11
Travel and transportation of persons.	140	134	175
Transportation of things.............	21	26	30
Rent, communications, and utilities..	354	246	400
Printing and reproduction............	350	350	395
Other services:			
Project contracts..................	1,234	1,209	1,263
Centrally furnished services.......	4,571	4,229	3,819
Standard level user charge.........	391	387	417
Other..............................	1,942	2,208	2,739
Supplies and materials...............	76	94	86
Equipment............................	135	185	152
Grants, subsidies, and contributions.	466,732	471,434	456,096
Total....................	481,624	486,206	471,533

NATIONAL INSTITUTES OF HEALTH

National Institute of General Medical Sciences

Authorizing Legislation

	PHS Act/ Other Citation	U.S. Code Citation	1986 Amt. Authorized	1986 Estimate	1987 Amt. Authorized	1987 Budget Request
Research and Investigation..........	Section 301	42 § 241	Indefinite	$431,204,000	Indefinite	$471,533,000
National Institute of General Medical Sciences..............	Section 461	42 § 285k 289h	Indefinite		Indefinite	
National Research Service Awards.........	Section 487	42 § 288	$244,000,000 1/	55,239,000	$260,000,000 1/	
Total Budget Authority.				486,443,000		471,533,000

1/ This training authority is shared with other research training programs of the National Institutes of Health; the Alcohol, Drug Abuse and Mental Health Administration; and the Health Resources and Services Administration.

National Institute of General Medical Sciences

Appropriations History

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation 1/
1978	220,341,000	225,796,000	235,400,000	230,796,000
1979	234,412,000	225,092,000	230,000,000	277,628,000
1980	280,528,000	312,478,000	304,000,000	312,468,000
1981	314,925,000	332,919,000	333,615,000	333,764,000
1982	300,257,000	2/ 360,561,000	354,138,000	339,862,000
1983	345,621,000	367,009,000	372,114,000	369,803,000
1984	383,139,000	363,444,000	3/ 370,245,000	3/ 415,937,000
1985	423,853,000	412,987,000	4/ 495,150,000	482,909,000
1985 Proposed Rescission	-211,000			
1986	458,484,000	455,593,000	5/ 510,872,000	514,765,000
1986 Sequester	-22,135,000			
1986 Proposed Rescission	-7,358,000			
1987	471,533,000			

1/ Reflects enacted supplementals, rescissions, and reappropriations.

2/ Reflects the September Amendment; the original request was $341,201,000.

3/ Excludes $48,000,000 in NRSA training programs not considered.

4/ Excludes $57,721,000 for NRSA training programs not considered.

5/ Excludes $57,721,000 in NRSA training programs not considered.

National Institute of General Medical Sciences
(Dollars in thousands)

Justification

	1986 Appropriation	1986 Available after Sequestering	1986 Revised		1987 Estimate	
	Amount	Amount	FTE	Amount	FTE	Amount
Cellular and molecular basis of disease.......	$146,856	$140,473	---	$138,213	---	$136,452
Genetics......	171,327	164,354	---	161,652	---	148,920
Pharmacological sciences......	74,366	71,057	---	69,958	---	70,147
Biophysics and physiological sciences......	101,263	96,167	---	94,870	---	94,774
Minority access to research careers.......	7,950	7,950	---	7,950	---	7,066
Intramural research......	875	837	21	837	21	875
Research management and support.......	13,299	12,726	139	12,726	139	13,299
Total.....	515,736	493,564	160	486,206	160	471,533

General Statement

The National Institute of General Medical Sciences (NIGMS) is unique among the National Institutes of Health in its mission to support basic, untargeted research in the biomedical sciences. In this context, "basic" signifies the fundamental nature of the studies supported by the NIGMS on such subjects as the structure and function of cell components, genetic principles, and the mechanisms of drug action. The findings gleaned from these kinds of investigations illuminate our understanding of life processes, and often have far-reaching clinical and technological applications. In this way, basic research can be viewed as the first, and perhaps most important, step in unlocking the mechanisms of disease processes. Without basic research, advances in medical treatment would slow down and eventually cease.

As early as the 1950's, basic investigations in cell biology, virology, and immunology were helping to develop the tools which now permit scientists to grow the AIDS virus in tissue culture for study. Similarly, fundamental studies of gene structure and function made possible the discovery and elucidation of genes involved in the development of cancer (oncogenes). The basic research being conducted today will be at the root of similar advances in the future.

A critical way in which basic research contributes to all science is in its development of new techniques and tools that facilitate further studies. Recombinant DNA technology — amazingly enough only 13 years old, despite its enormous impact on research, medical care, industry, and agriculture — is but one example. Another is the instruments, like sophisticated microscopes and powerful computers, that have made it possible for biophysicists — scientists who apply the principles of physics to the study of biological phenomena — to examine detailed molecular structures. For instance, a team working with NIGMS support recently became the first group to "map" the detailed structure of an animal virus — in this case, a human cold virus. The knowledge gained through this research may someday enable scientists to find ways to fight the common cold. Moreover, the technology developed in the course of this work can now be applied to the study of the atomic structure of a variety of other disease-causing viruses and other molecules.

NIGMS supports basic, non-disease-targeted studies through four research programs: Cellular and Molecular Basis of Disease, Genetics, Pharmacological Sciences, and Biophysics and Physiological Sciences. In all of these areas, NIGMS has as its main mission the provision of new knowledge, theories, and concepts that undergird the disease-targeted studies supported by other components of the National Institutes of Health.

Recent studies by NIGMS grantee Dr. David Feldman of Stanford University illustrate well the wide-ranging impact of a single line of inquiry in basic research. A few years ago, Dr. Feldman and his colleagues made the surprising discovery that several types of yeast — some of which can cause infections in humans — produce both a protein that recognizes and binds to specific molecules as a receptor and a substance that binds to the "receptor" in a hormone-like way.

The scientists were mystified: What use could a yeast possibly have for a hormone? In higher animals, hormones are secreted by glands in one part of the body and carried by body fluids to affect specifically receptive organs or tissues in other parts of the body. But, what could hormones do for a one-celled organism? Some scientists hypothesize that hormones in certain yeasts may play a role in intercellular signaling, and that in the past such signaling between one-celled organisms has been a crucial step in the development of multicellular animals. The extracellular fluid in which the one-celled organisms lived could thus be seen as a precursor to the bloodstream.

Discovery of these different types of hormone activity in yeast (which is a kind of fungus) led Dr. Feldman to examine the mechanisms of action of the drug ketoconazole, an oral antifungal medication. He found that this drug works, in part, by inhibiting the body's synthesis of steroid hormones. At about the same time, reports were coming from Britain of increased death rates in an intensive care unit in which the drug etomidate began to be used as a sedative for patients on respirators. Because Dr. Feldman knew that there were similarities between etomidate and ketoconazole, he decided to see if etomidate might also inhibit steroid synthesis, and indeed found this to be the case.

It is, of course, well known that patients hospitalized for injuries or undergoing operations are already under stress. Suppression of the ability to produce steroids, such as seems to be associated with etomidate, decreases tolerance to stresses like hemorrhage or infection and may place a patient at increased risk, should complications occur. Thus, Dr. Feldman's studies have provided information vital to physicians and anesthesiologists, information, in fact, of a life-saving nature -- an unpredicted result of work that started with basic research on yeast.

The NIGMS also supports research training aimed at providing the highly qualified, creative personnel necessary to realize the scientific promise of the future. Each of the programs named above has a research training component; in addition, NIGMS has a fifth program devoted solely to training: the Minority Access to Research Careers (MARC) Program. The role of the NIGMS in the training of future researchers is vital to meeting the needs of both academic research and the rapidly expanding biotechnology industry.

The MARC Program and another special training effort by NIGMS, the Medical Scientist Training Program (MSTP), are designed to rectify personnel shortages in specific areas. As its name indicates, the MARC Program seeks to increase the number of biomedical scientists from minority groups. The MSTP, which just celebrated its 20th anniversary, addresses the pressing need for well-trained clinical researchers by supporting outstanding students who are working toward the combined M.D.-Ph.D. degree. In 1985, this program funded 683 student positions at 25 top medical schools.

Several recent studies of the MARC Program have confirmed prior anecdotal evidence that it is meeting its goals. The latest study, conducted by the Institute of Medicine of the National Academy of Sciences, focused on the primary component of MARC, the Honors Undergraduate Research Training Program.

It found that a steadily increasing number of MARC-supported biology majors go on to graduate studies, and ultimately find work in science fields.

Over the years, the NIGMS has supported the work of a substantial number of Nobel Prize and other award-winning scientists. This past year was no exception. The recipients of the 1985 Nobel Prize in Physiology or Medicine and the 1985 Albert Lasker Basic Medical Research Award, Drs. Joseph L. Goldstein and Michael S. Brown of the University of Texas Health Science Center at Dallas, were investigators on two NIGMS grants from 1972 to 1977. During this period, they made the fundamental discovery of receptors involved in cholesterol metabolism, work that was called "a milestone" by the Nobel Committee in its announcement of that prize.

NIGMS also provided support to Dr. Herbert A. Hauptman of the Medical Foundation of Buffalo, who shared the 1985 Nobel Prize in Chemistry with Dr. [illegible] Karle of the U.S. Naval Research Laboratory. These scientists received the award for developing mathematical techniques to determine the three-dimensional structures of small molecules in a much more rapid and direct way than was previously possible. Knowledge of the detailed structure of molecules has important implications for the development of new drugs, as well as for understanding how biological substances, such as hormones, function in the body. The approach taken by Drs. Hauptman and Karle greatly improves the information that can be obtained from X-ray crystallography, a technique that provides structural data about molecules by passing X-rays through crystals of molecules and recording on film how these molecules scatter light. The analysis of these patterns of diffraction was extremely difficult, time-consuming, and often inexact until Drs. Hauptman and Karle devised formulas for comparing the relative intensities of the spots of diffracted light. With the aid of powerful computers, analyses now can be done in a matter of days, rather than years, as had beem true in the past.

As the program accomplishments that follow will attest, basic biomedical research is probably the most exciting area of scientific investigation being pursued today. Studies that are not targeted to the problems of a particular disease have enormously increased our knowledge and our capability for further study of life's most fundamental puzzles. However, since there is much to know and progress builds on progress, the future promises even greater advances.

Overall Budget Policy

The NIGMS budget request for 1987 continues to emphasize the support of investigator-initiated research project grants and the training of future researchers. The budget request is $471,533,000, which represents a decrease of $14,673,000 from the 1986 revised estimate.

These levels will be achieved by limiting indirect cost and by negotiating direct costs downward. The request will support 689 competing project grants at an average cost of $146,400. This represents a 2.1 percent decrease in direct costs over 1986 and an 8.6 percent reduction from full recommended levels. Historically, these reductions have averaged 3 to 4 percent. The request will support 2,082 noncompeting project grants at an average cost of $140,500. This represents a 2.2 percent decrease in direct costs over 1986 and a 9.6 percent reduction from full commitment levels. Historically, these reductions have averaged 1 percent.

The request will fund 11 research centers in 1987, a reduction of four from the 1986 revised estimate. This represents a 13 percent reduction from full recommended costs compared to a .8 percent reduction in 1986.

Moreover, the 1987 request will provide support for 2,797 trainees, a reduction of 311 from the 1986 revised estimate.

The request will support mandatory changes and increased costs of ongoing activities in Intramural Research and Research Management and Support.

Program Accomplishments

Among the most noteworthy research advances supported by NIGMS are the following:

1. As has happened several times in the past few years, an NIGMS grantee studying fundamental genetic processes has discovered an exception to a rule that was previously assumed to apply to every living creature on earth. Dr. John Preer, Jr., of Indiana University in Bloomington was one of a number of scientists who found that the genetic code -- the blueprint by which information held in the genetic material, DNA and RNA, is translated into protein products -- is slightly different in a type of single-celled organism called a ciliated protozoan. A sequence of genetic information that in most organisms signifies "stop making protein" instead specifies the production of a specific amino acid (protein building block), glutamine, in this protozoan. Prior to this finding, scientists thought that the genetic code was universal; that is, a given sequence held the same information regardless of the organism in which it existed. In fact, the majority of organisms do share a common genetic code — this is what makes the use of the recombinant DNA techniques so successful. But the finding of such an exception raises many questions that can only be answered by further studies in this area, which will provide new clues about the development of the genetic code.

2. Dr. David S. Hogness of Stanford University and other NIGMS grantees have been instrumental in developing an important new method for determining the chromosomal location of a gene. Before this technique was available, a scientist had to know what protein product was specified by a particular gene in order to find the gene itself. Unfortunately, the primary protein defect has not been identified in many major genetic disorders, such as cystic fibrosis, making it impossible to use this method to search for the gene or genes responsible for these diseases. The new technique allows researchers to locate and isolate genes for which the protein products are not yet known. This approach has already led to the discovery of markers associated with the genes responsible for Huntington's disease and cystic fibrosis. Such markers may form the basis of diagnostic screening tests to determine the presence of the disease, either pre- or postnatally.

3. NIGMS-supported scientists are studying calcium, an element that is essential for the normal functioning of most living cells. Such processes as blood clotting and muscle contraction are dependent upon the presence of calcium. Moreover, numerous enzymes and hormones require calcium in order to be biologically active. The researchers, who include Dr. Daniel Watterson at Vanderbilt University and Dr. Roger Tsien of the University of California, Berkeley, are making new discoveries about the mechanism of calcium action and

the role it plays in regulating cellular processes. Their findings will shed light on this important aspect of cell biology, and may have implications for the treatment of disorders involving defects in calcium function at the cellular level.

4. Respiration, the processing of energy-rich "fuel" molecules to provide cellular energy, is an extremely complex event in higher organisms and thus has proved difficult to study. Now, however, Dr. Bernard Trumpower of Dartmouth Medical School has found a simple respiratory system in the membrane surrounding the bacterium Paracoccus denitrificans. This system appears to be functionally identical to that of mitochondria, the organelles responsible for respiration in eukaryotic cells (the cells of a large class of organisms that includes mammals). The system, which Dr. Trumpower is now working to perfect, should become an excellent model in which to study the molecular basis of the vital process of respiration in higher organisms.

5. With NIGMS support, researchers have shed new light on the biochemical basis of the "wasting syndrome" (the development of severe weakness and loss of weight). This is caused by certain infections, injuries, and cancers. Dr. Gordon M. Ringold and his colleagues at the Stanford University School of Medicine have found that a protein, cachectin, which is produced in response to severe physiological stress, causes fat cells to release energy and prevents them from storing fat from food sources. While an initial burst of energy stimulated by cachectin has obvious value in fighting infections or injuries, the inability to maintain fat supplies can be debilitating and dangerous. Improved understanding of the mechanism of action of this protein should help scientists devise means for preventing chronic wasting, and may also have implications for treating obesity. Interestingly, other scientists (one of whom is an NIGMS grantee) have found that cachectin is identical to tumor necrosis factor, a protein now being tested for its anticancer properties.

6. A report by the National Science Board on the state of U.S. science, engineering, and technology identifies research by long-time NIGMS grantees Dr. Donald Cram of the University of California, Los Angeles, and Dr. Ronald Breslow of Columbia University as one of eight "recent and significant achievements of scientific and engineering research." Both scientists are involved in efforts to design a variety of artificial molecules with the catalytic properties of natural enzymes. Dr. Cram has approached this by creating molecules with cavities that bind target substances and that have chemical groups arranged in such a way that they speed up the rate of a specific reaction in the bound substance. Dr. Breslow has taken cavity-containing molecules and chemically modified them so they approach the catalytic power of natural enzymes. While these efforts are still fairly preliminary, they hold a great deal of promise for eventually enabling scientists to develop artificial enzymes that function with an efficiency approaching that of enzymes found in nature, and may be important for specific medical and technological purposes.

7. Basic studies of the scattering of light by cells have led to a technique that has the potential for identifying disease-causing microorganisms much more rapidly than is now possible. The system, developed by Dr. Gary R. Salzman of the Los Alamos National Laboratory, is based on the interaction of a microorganism's genetic material with polarized light from

different directions. Since the organisms do not have to be isolated and cultured, testing can be done in minutes rather than hours or days. The shortened time it will take to make a diagnosis using this technique should prove valuable in the treatment of many diseases, including spinal meningitis, septicemia, pneumonic plague, and Legionnaire's disease, illnesses for which prompt diagnosis is particularly important for therapy to be effective. Dr. Salzman is planning improvements in the system to enable it to identify and estimate the relative quantity of each type of microorganism in samples that contain many different types of organisms, as do most clinical specimens. The device is expected to be marketed by a private firm for clinical use within the next few years.

8. In an effort to find ways to speed up and improve wound healing, many NIGMS grantees are examining the basic processes involved. In one study, Dr. Thomas Hunt of the University of California, San Francisco, is looking at the relationship of oxygen to the healing process. It is well known that wounds heal better and resist infection more effectively if their blood and oxygen supplies are good. However, in the past there has been no satisfactory way of measuring oxygen supply to tissues. Dr. Hunt and his colleagues have now patented a simple device for measuring oxygen tension in human tissue. The device, which resembles an intravenous needle, has been used in several hundred patients and has proved extremely valuable in deciding when blood transfusions or other fluids are necessary. Studies by these researchers, utilizing the device, have shown that exposure of guinea pigs to high levels of oxygen, especially during the first 4 hours after infection, greatly increased the ability of animals to retard bacterial growth.

National Institute of General Medical Sciences

Cellular and Molecular Basis of Disease

1987 Authorization: Indefinite.

Obligational Authority:

1986 Appropriation	1986 Available after sequestering	1986 Revised Estimate	1987	Increase or decrease
$146,856,000	$140,473,000	$138,213,000	$136,452,000	-$1,761,000

Purpose and Method of Operation

The cell is the fundamental biological unit of all living organisms. It holds the capacity for generating, from simple exogenous sources, all its macromolecules (e.g., proteins, RNA and DNA), energy, and complex organization and structure. The Cellular and Molecular Basis of Disease (CMBD) Program is concerned with basic questions about the functions of cells and their components. The research and research training supported by this program encompass a wide range of scientific efforts, from cell-cell communication, cell adhesion, and development, to cellular metabolism, energetics, mechanisms of enzyme action, and the molecular structure of cells. Ranging as it does from the molecular to the multicellular, this research is broad in scope, and utilizes a wide variety of both traditional and emerging technologies, instruments, and models. Results from this basic cellular and molecular research continue to contribute to our expanding knowledge about how a healthy body functions and why disease occurs.

Recognition of this contribution came again this year in the award of the 1985 Nobel Prize for Physiology or Medicine to Doctors Michael Brown and Joseph Goldstein, whose early work was supported by NIGMS. Brown and Goldstein's investigation of cholesterol uptake in cell cultures began by investigating how cholesterol molecules get from the circulatory system into the cell. They tracked the molecules to cell membranes and found that they attached to specialized receptors clustered in coated "pits" on the surface. They saw that when the receptors had collected their quota of cholesterol molecules, the "pits" were pinched into the cell, forming vesicles. Enzyme activity inside the cholesterol-laden vesicles then freed the cholesterol from the receptors and released it into the cell. The receptors then were recycled back to the cell surface when the cellular supply of cholesterol fell short of the required amount. This early work on cholesterol receptors by Doctors Brown and Goldstein led to their important investigations of the genetic basis of, and potential therapies for, familial hypercholesterolemia, a serious and often fatal genetic disorder tied to defects in these receptors. Furthermore, their discovery of the activity of cholesterol receptors opened the door to numerous basic studies of how other important proteins are brought into the cell via membrane receptors.

The CMBD Program supports a good deal of such receptor research, including studies of receptors which, like the cholesterol receptors, serve the function of recognizing and internalizing or transporting molecules that the cell needs. For example, support is provided for studies of the receptors in liver cells which gather asialylglycoprotein, a blood protein that deteriorates and becomes useless as it ages, and must be cleared from the blood. Other scientists supported by the CMBD Program are investigating how the receptors in the membranes of the cells lining the intestines recognize and then transport the amino acids critical to the digestive process.

Still other grantees of the CMBD Program are examining the receptors which perform a second important function — namely, receiving and transmitting the "signal" molecules that influence or control cell activity. Among the most important of such receptor research studies are those examining the receptors for epidermal growth factor (EGF). EGF appears to be an important member of a group of peptides that play a role in controlling cell division. Interest in EGF is intensifying because of evidence that: (1) it is similar to a number of transforming growth factors that are believed to be oncogene products, and (2) the EGF receptor is identical to another oncogene product. Thus, studies of the epidermal growth factor receptors may have far-reaching implications not only for normal cells, but also for their transformation into malignant cells.

This research on receptors is illustrative of the CMBD-supported studies of many cellular and molecular structures and processes which are fundamental to health. The mysteries surrounding the proper position of receptors, how they recognize the molecules to which they attach, how they transport those molecules, and how their activity triggers both normal and abnormal cellular events, are not unlike the questions that basic scientists are exploring regarding the nature and function of the cells themselves, as well as of other cellular components. Research funded by the CMBD Program has produced a number of important findings during the past year, among them:

- Monoclonal antibodies have been used, along with other techniques, to identify which of the several glycoproteins (sugar-protein complexes) that coat the herpes simplex viruses might play a key role in permitting such viruses to penetrate the host's cells, and which of them might also be the trigger for the host's immune response to these herpes viruses. This research may facilitate the development of successful treatment regimens for a number of conditions caused by herpes simplex -- such as cold sores, genital herpes, and a form of encephalitis.

- Important progress has been made in explorations of bacteriorhodopsin, an excellent model to investigate the structure and function of human rhodopsin, the pigment in the rods (specialized cells) of the retina which is responsible for the first step in vision, namely converting light energy into a chemical signal. The gene responsible for coding the protein bacteriorhodopsin has been sequenced and numerous details of the protein's structure and function elucidated. This work in a bacterial model has begun to impact not only on research on human rhodopsin, but also across a wide range of other studies on bioenergetics. It has implications, also, for various biotechnological applications.

- Scientists have developed a new method to block the gap junction channels in cell membranes. These gap junction channels are the conduits of the signals involved for cell-to-cell communication. Unlike the method previously employed by scientists, which used calcium to block the channels but in so doing perturbed numerous other calcium-dependent cell functions, the new method uses antibodies which can very selectively block these gap junction channels. This permits more precise investigations of the role of cell-to-cell communication. For instance, blocking certain of these channels in the embryonic cells of frogs may result in specific birth defects. This suggests that the blocking technique may have useful applications in the exploration of the causes of birth defects.

- Scientists have done preliminary work isolating and identifying a protein in liver cell membranes which is the site of the liver cells' attachment to its extracellular matrix. This has been particularly painstaking work, but is of major importance because other research has clearly demonstrated that cell adhesion or attachment plays a role in controlling cell growth and in proper tissue formation; and, when it goes awry, in permitting uncontrolled cancer cell growth.

The CMBD Program supports investigator-initiated research projects, research centers, research contracts, and research training in the form of both individual and institutional fellowship awards.

Rationale for the Budget Request

The 1987 request of $136,452,000 for Cellular and Molecular Basis of Disease Program represents a decrease of $1,761,000 from the 1986 revised estimate. This request will provide for 818 research project grants, 1 research center, 3 other research awards, 1,241 trainees, and 2 research and development contracts.

In 1987, the CMBD Program will support research in a number of promising areas, including the following:

1. Membrane Structure and Function: All cells are bounded by a plasma membrane which controls the movement of substances in and out of the cell. In addition, intracellular membranes form compartments such as the nucleus, mitochondria, or Golgi apparatus which delineate cell components with specific functions. Because membranes are dynamic "boundaries" for cells and their organelles, they play a central role in cell physiology, particularly in such processes as growth control, hormone action, and cell energetics. Membrane research is the largest and most rapidly expanding area within CMBD. The most exciting new work is occurring in three major areas of study which have greatly expanded our understanding of: the mechanisms by which proteins are inserted into their proper membrane location; the biochemical pathways by which membrane constituents are recycled; and the chemistry of membrane receptors which control the transport of specific molecules across membranes.

2. Cell Growth and Differentiation: In many ways, research at the level of the cell or tissue is the most difficult because the systems involved are so complicated and the variables hard to understand or to control. Yet, clearly, research on the cell cycle, particularly on the processes of cell growth and differentiation, is important to furthering our understanding of both healthy and abnormal development. Not only are investigations exploring the genetic and microenvironmental regulation of cell differentiation into the many tissue types and organs characteristic of mature organisms, but other studies are also examining the processes influencing development of cell organelles (the structures inside cells which perform specialized cellular functions vital to normal physiology). While research in these areas is burgeoning, two examples may demonstrate the opportunities and importance of this work. One exciting area is that of stress or heat shock proteins. Several laboratories are making excellent progress in purifying stress proteins. These proteins play an important role in regulating protein synthesis in general, and thus are of great interest in the study of the control of gene expression. Another, although extracellular, protein involved in growth control is platelet-derived growth factor (PDGF). Grantees are studying induction of a gene called c-myc by PDGF. This gene may play an important role in cell proliferation.

3. Molecular Immunobiology: Alterations in the body's immune response have far-reaching implications for a variety of diseases, including cancer, immunodeficiencies, and autoimmune disorders. Furthermore, cells of the immune system, and their products, provide excellent models for addressing basic questions in cellular and molecular biology, such as the nature of complex cell interactions, the developmentally controlled expression of groups of genes, and the mechanisms of cell activation and differentiation. CMBD supports an expanding interdisciplinary subprogram in molecular immunobiology with emphasis on these basic cellular processes. Active areas of research include regulation of the cell cycle by lymphocyte growth factors, transmembrane signaling via immunocyte receptors, and the structure, function, and genetic basis for the expression of key molecules related to the immune response (e.g., antibodies).

4. Multifunctional Enzymes: Enzymes are the highly efficient catalysts for the chemical reactions that are central to the processes of living cells. Structurally, these catalysts are proteins possessing a particular site that recognizes a target molecule, binds it, and changes it in some way; typically, these catalytic proteins possess one such site and thus have one enzymatic function. However, it is becoming apparent that there are some proteins that possess a number of different catalytic sites. These substances, known as multifunctional enzymes, carry out all, or at least many, of the reactions in a given metabolic pathway. For example, the multifunctional enzyme, fatty acid synthetase, effects a seven-step series of reactions that yields the fatty acid, palmitate, which is an important structural component of cell membranes. The importance of multifunctional enzymes is generally thought to reside in the enhanced metabolic efficiency that they provide. It is also thought that incorporating numerous enzymatic functions into one protein allows the cell to regulate a number of enzyme activities (or, indeed, an entire metabolic pathway) coordinately. Investigators, supported through the CMBD Program, are examining multifunctional enzymes in an effort to answer a number of fundamental questions: How is the protein chain folded so that multiple functional sites can be maintained? To what extent are the

functional sites independent? How are the amounts of these enzymes regulated within the cell? What are the kinetics and chemical mechanisms of the reactions facilitated by these multifunctional enzymes?

5. Bioenergetics: All cells, from the simplest unicellular bacteria to those of man, possess the ability to obtain energy from their environment; the energy may come from sunlight, as is the case for plants, or from ingested foods. Regardless of the source, cells must convert the energy derived from the environment to a usable form. The form that is almost universally used by cells is the chemical energy found in a molecule known as adenosine triphosphate, or ATP. The high-energy ATP molecule is used by cells to "drive" a wide range of processes, such as cellular movement, the transport of material in and out of the cell, and the manufacture of crucial cellular components such as enzymes, membranes, and various sensory processes. The cellular conversion process whereby food or light is converted into ATP is generally quite complex; indeed, in all higher organisms the apparatus used for this conversion involves scores of membrane-bound proteins that, for a variety of reasons, have been difficult to study. Despite these difficulties, investigators are making progress in understanding the structural and functional details of the mammalian apparatus. One approach that is particularly promising is the study of the conversion apparatus of bacteria, which, while similar in function, is considerably simpler in structure.

Studies with these simple "model" systems, which to some extent rely on recombinant DNA techniques, should allow investigators to make further progress in understanding this central cellular process.

Cellular and Molecular Basis of Disease

Impact Data	1986 Appropriation	1986 Available after Sequestering	1986 Revised Estimate	1987 Estimate
Res. proj. grants				
Number	868	868	824	818
Amount	$123,617,000	$118,277,000	$116,017,000	$113,815,000
Res. centers				
Number	1	1	1	1
Amount	918,000	918,000	918,000	799,000
Other res.				
Number	6	4	4	3
Amount	240,000	192,000	192,000	182,000
Training				
FTTP	1,324	1,265	1,265	1,241
Amount	22,016,000	21,021,000	21,021,000	21,591,000
Res. and dev. contracts				
Number	2	2	2	2
Amount	65,000	65,000	65,000	65,000
Total	146,856,000	140,473,000	138,213,000	136,452,000

National Institute of General Medical Sciences

Genetics

1987 Authorization: Indefinite.

Obligational Authority:

1986 Appropriation	1986 Available after sequestering	1986 Revised Estimate	1987	Increase or decrease
$171,327,000	$164,354,000	$161,652,000	$148,920,000	-$12,732,000

Purpose and Method of Operation

The Genetics Program is responsible for providing financial support for basic research studies concerned with elucidating the fundamental mechanisms of inheritance. Such research is designed to develop information needed by researchers seeking to discover effective methods for the diagnosis, treatment, and prevention of the more than 3,000 genetic disorders which are known to afflict mankind.

Genetic disorders account for a major portion of the diseases and deaths recorded in the United States each year, with an estimated 6 percent of the U.S. population suffering from a genetic disorder which can be described as severe. Illustrative is the case of Lesch-Nyhan syndrome, an inherited disease brought on by the presence of a simple defect in just one of the estimated 100,000 genes possessed by humans. This inherited defect prevents the normal production by the body of an enzyme called HPRT (hypoxanthine-guaninephosphoribosyl transferase), which is needed to metabolize (break down) chemicals which are present in all of us. These chemicals must be broken down to be eliminated, thus preventing abnormal buildup. Because of the lack of HPRT, crystals of uric acid collect in the kidneys and joints of the victims of this disease, with disastrous consequences. Victims tend to be mentally retarded; they have to be restrained to avoid self-mutilation (they often chew off their own fingers); and they seldom live beyond their 20th birthday. Other inherited disorders (e.g., Down's syndrome, cystic fibrosis, Tay-Sachs disease, Huntington's disease, and sickle cell anemia), many of which are also caused by a single genetic defect, have similarly devastating effects — destroying both individuals and families, while placing an enormous financial burden on our health care system. Indeed, an estimated 15-20 percent of all health care costs are associated in some way with genetic disease.

Despite the gravity of this situation, there are, as yet, relatively few genetic disorders which can be diagnosed prior to the onset of symptoms; and while some of these symptoms can be treated if recognized early enough, there is still no way to "cure" a genetic disorder. This would require the ability to identify the site of a defective gene, and then either the ability to replace it or repair it -- a goal still beyond the reach of modern medicine.

There has been great progress, however, with regard to the development of methods for pinpointing the chromosomal sites of defective genes, an effort led by many dedicated teams of researchers throughout the country, most of whom receive Genetics Program support. At last count, over 400 human genes have been definitely "mapped," with another 400 tentatively "mapped," or localized to specific areas of chromosomes. Almost 200 of these genes, when abnormal, are known to cause human disease. Such gene mapping represents a key step toward the development of better methods for diagnosing genetic diseases, as well as toward developing effective methods of treatment. Most recently, a "marker" was discovered for the gene responsible for cystic fibrosis, a usually fatal disease which afflicts an estimated 30,000 Americans. This finding narrows the search for the exact site of this gene to just one percent of the total human DNA, providing hope for many American families.

Significant progress has also been made on other important fronts, with genetic researchers learning more and more, for example, about the molecular machinery which works to turn genes on and off at just the right moments -- as well as the nature of the consequences when such machinery goes awry. One important area of study here has been the operation of "heat shock genes" which "turn on" in response to high temperatures to produce specialized proteins needed by the body to protect itself. Scientists are hopeful that they can eventually use the information obtained from such studies to gain an understanding of how the functioning of all genes is regulated. It is believed that this, in turn, will facilitate efforts to control the effects of genetic disorders.

During the past year, important discoveries were made by grantees of the Genetics Program in the following areas:

- Utilizing a small, transparent roundworm with a life cycle of only 3.5 days as a model, researchers at the Massachusetts Institute of Technology were able to determine the specific effects of a mutant gene that affects the timing of cell division on the production of certain kinds of developmental defects.

- Investigators at Stanford University made important improvements to a methodology which they developed in 1981, designed to allow test-tube studies of DNA replication, the process by which genetic information is passed on from generation to generation. Their success will dramatically speed up studies in this critical area.

- A researcher at the University of Florida has shed new light on the mechanisms involved in genetic recombination (the process by which strands of DNA exchange genetic material). His discoveries are extremely important because of the key role recombination plays in the development of genetic variations, as well as its role in many cell functions.

- Researchers at Duke University have discovered a mechanism by which the body manages to repair mismatches which occasionally occur in the genetic codes of duplicate DNA strands. Their findings have stimulated much study on the subject of natural repair systems and have encouraged scientists to develop some specific, testable models of how mismatch repair is accomplished.

Support under this program is provided through the use of investigator-initiated research grants, research center grants, R & D contracts, and both individual and institutional fellowship awards.

Rationale for the Budget Request

The 1987 request of $148,920,000 for the Genetics Program represents a decrease of $12,732,000 from the 1986 revised estimate. This request will provide for 940 research project grants, 2 research centers, 7 other research awards, 104 trainees, and 3 research and development contracts.

The Genetics Program will provide special emphasis to the following program areas in 1987:

1. Developmental Genetics: Genetics researchers have long sought to understand how cells which develop from a single fertilized egg manage to differentiate into the various specialized cell types which form tissues and organs, especially since it has been recognized for some time that each specialized cell contains all of the same genes possessed by its parent cell. The key to this riddle now appears to be in the action of recently discovered "developmental genes," which switch on and off at critical times to control the way in which a cell and its progeny develop. Genetics Program grantees will continue to explore this subject over the next year, with an eye toward gaining a better understanding of how developmental errors occur, thereby laying the groundwork for preventing them.

2. Chromosome Organization and Mechanics: A considerable amount of data has been generated in recent years concerning the effects of variations which exist in chromosomal architecture. Genetics Program grantees have discovered, for example, that the eye color inherited by a fruit fly is directly influenced by three separate factors: the information carried by its eye-color gene, the gene's location on the fruit fly's chromosome, and the location of the cells carrying the gene in the eye. When located at any of more than 20 sites on the chromosome, the standard fruit fly eye color gene will produce red eye pigmentation. But, at two other locations, the same gene produces abnormal pigmentation patterns--flecks of red on a yellow background at one location and areas of light and dark pigmentation at the other, leading to the conclusion that mutant expression can be affected by the surrounding chromosomal region in which the gene is inserted. Studies of this kind provide vital information to researchers regarding the specific mechanisms involved in the process of inheritance, and also help to explain the occurrence of mutations which result in genetic disorders. The Genetics Program will continue to emphasize research on chromosome organization and mechanics in 1987, including research on the effects of different nucleotide sequences in chromosomes; the effects of changes in sequence distribution and organization during development and differentiation; and studies of the mechanisms involved in chromosomal rearrangements.

3. Gene Mapping: As noted above, gene mapping, the process of identifying the specific chromosomal locations of genes responsible for

particular inherited characteristics, including inherited disorders, is currently a major preoccupation within the genetic research community. The reason is simple. If they are to have any chance at all of correcting a genetic defect, investigators must first pinpoint its location. Within the past year, Genetics Program grantees were able to localize to a site on human chromosome 19, the gene responsible for the production of human insulin receptors, receptors on the outer cell membrane which must be produced by the body in just the right quantities to avoid the occurrence of certain types of diabetes. Also of interest, however, is the observation by the researchers involved that the site on which the human insulin receptor gene is located is the same one involved in a certain form of leukemia, suggesting that this gene could function as an oncogene (cancer-causing gene) under certain conditions—for example, conditions leading to chromosomal rearrangements which might alter its expression.

Gene mapping will continue to be a high priority activity supported by the Genetics Program in 1987, with efforts being made both to develop improved techniques and to fill in many of the blank spaces still remaining on the gene map currently available. Typical will be efforts to map the genetic defect responsible for many X chromosome-linked diseases, including Duchenne muscular dystrophy and fragile X-linked mental retardation.

4. Gene Therapy: The ultimate goal of genetics research remains the ability to cure inherited diseases. Many problems must be overcome, however, before physicians can "fix" a defective gene or replace it with a new, normally functioning one. Safe and reliable "gene replacement therapy" would require, for example, that the inserted normal gene line up with and specifically replace only the defective gene. Otherwise, the treatment might cause a variety of disastrous side effects, perhaps causing normal genes to malfunction. A significant breakthrough, in this regard, was achieved during the past year by an NIGMS grantee at the University of Wisconsin, who successfully inserted a beta-globin gene into a predetermined site in a human chromosome. His experiments have clearly established the fact that a planned modification of a specific human gene is possible without disrupting the remainder of the genome, and also open up the possibility of one day inserting beta-globin genes in a planned fashion as part of a new, effective treatment for such genetic diseases as beta-thalassemia and sickle cell anemia, both globin-related disorders. Research focusing on a wide variety of preliminary approaches to gene therapy will be supported in 1987.

5. Extranuclear Inheritance: Until recently, it was thought that all the genetic information passed on from generation to generation was contained in the chromosomes of a cell's nucleus. It is now understood, however, that the mitochondria (the cellular organs responsible for respiration) contain their own DNA, raising the possibility that a number of genetic diseases exist which can be traced to defects in mitochondrial, rather than in nuclear, DNA. Further research to delineate the functions of mitochondrial genes is therefore a topic of great interest within the scientific community. Within the past year, Genetics Program grantees have identified six new genes in the human mitochondrial genome, and studies in this area will continue.

Genetics

Impact Data	1986 Appropriation	1986 Available after Sequestering	1986 Revised Estimate	1987 Estimate
Res. proj. grants				
Number	1,002	1,002	955	940
Amount	$161,671,000	$155,294,000	$152,592,000	$143,317,000
Res. centers				
Number	3	3	3	2
Amount	2,784,000	2,784,000	2,784,000	1,621,000
Other res.				
Number	12	10	10	7
Amount	364,000	315,000	315,000	254,000
Training				
FTTP	216	197	197	104
Amount	5,310,000	4,817,000	4,817,000	2,530,000
Res. and dev. contracts				
Number	3	3	3	3
Amount	1,198,000	1,144,000	1,144,000	1,198,000
Total	171,327,000	164,354,000	161,652,000	148,920,000

National Institute of General Medical Sciences

Pharmacological Sciences

1987 Authorization: Indefinite.

Obligational Authority:

1986 Appropriation	1986 Available after sequestering	1986 Revised Estimate	1987	Increase or decrease
$74,366,000	$71,057,000	$69,958,000	$70,147,000	+$189,000

Purpose and Method of Operation

The Pharmacological Sciences (PS) Program supports a broad spectrum of research aimed at providing an improved understanding of the biological phenomena and related chemical and molecular processes involved in the actions of therapeutic drugs and anesthetics. The scope of the program ranges from chemical syntheses and molecular pharmacology to controlled studies of the effects of drugs in man. Much of the research supported by the Program integrates such fields as genetics, endocrinology, chemistry, and computer science with the more traditional areas of pharmacological investigation in an effort to characterize molecular interactions and to understand their expression in man. While substantial portions of the PS Program budget support work in anesthesiology and pharmacology, the most significant expenditures are for research in biorelated chemistry. Within this broad field, research in basic chemistry predominates — in recognition of the importance of such work to the design and synthesis of a wide variety of compounds of potential health-related use.

A major thrust of the basic research supported by the Pharmacological Sciences Program is concerned with determining how pharmacologically active substances exert their effects, so that side effects can be minimized and new and better drugs can be developed. Part of this effort involves elucidating the structure of particular compounds that have been found to be useful as drugs. Once the structure has been defined, it can be modified in attempts to design more potent drugs, drugs with the desired therapeutic action but not the side effects, or drugs to which organisms have not yet developed resistance.

An example of this continuing process is the development of beta-lactam antibiotics, which include the penicillins and the cephalosporins. Naturally occurring beta-lactam antibiotics were discovered many years ago and currently are among the most widely used antibiotics. They are manufactured in multi-ton quantities annually by the drug industry, generally by isolating specific compounds from fermentation broths and then chemically modifying them to yield the desired characteristics. Scientists are searching continuously for new, structurally different beta-lactam antibiotics, because bacteria continue to develop resistance to those traditionally prescribed. Recently, an NIGMS-supported investigator discovered a totally new approach to beta-lactam synthesis. This reaction proceeds at room temperature, under mild reaction conditions, and is catalyzed (enhanced) by sunlight. The reaction is very versatile and can involve a wide range of functional groups. After further research, when this synthetic procedure is fully developed, it could be of profound utility for the efficient synthesis of completely new classes of beta-lactam antibiotics.

Many new therapeutically important or promising compounds have structures containing several chemical "rings." However, these have been difficult to synthesize in the laboratory or the factory. Recent discoveries by NIGMS grantees have simplified such synthesis greatly. One promising new approach for making such rings involves the use of a novel silicon reagent and a special catalytic template that helps to position the atoms correctly so that ring formation can occur more easily. Techniques such as these have been used so far to synthesize compounds containing five-membered rings, such as loganin, an important biosynthetic intermediate that has been used in folk medicine, and six-membered rings such as steroids that may be useful as hormones for treating inflammatory diseases and infertility.

In efforts to improve procedures for the large-scale synthesis of pharmacological agents, some investigators are making use of enzymes (naturally occurring catalysts) in order to synthesize useful compounds more efficiently. This approach involves one or more enzymes and may combine enzyme-catalyzed reactions with nonenzymatic reactions. One advantage of this approach is that many enzymes can catalyze very specific reactions in more than one compound, naturally occurring or not, and under very mild conditions. Enzymes have been employed for the synthesis of naturally occurring amino acids, as well as new ones, and can be used for preparing pharmacologically important compounds such as L-dopa, used for treating Parkinsonism. Other enzymes are used to generate high-energy compounds, such as adenosine triphosphate (ATP), which then can be employed to produce additional new compounds, such as sugar phosphates.

All these research efforts have the potential both of increasing the efficacy of therapeutic agents and of improving the efficiency with which pharmaceutical companies can manufacture these agents.

In the past year, the following significant advances were made by grantees of the Pharmacological Sciences Program:

- Nobel Laureate Dr. Herbert Brown has discovered a general method for synthesizing, with 100-percent purity, either one of the partners of any therapeutic compound that exists normally in two configurations which are mirror images of one another. Since usually only one of the two configurations has therapeutic activity, and the other may have toxic effects, this new method has immense practical significance. Until now, procedures for making these compounds have produced a mixture of both the active and inactive partners. By producing only the active, therapeutic compound, this method should minimize unwanted drug side effects.

- The ability to metabolize organophosphate compounds, such as certain insecticides and drugs, differs among people. Research to determine the genetic basis of this variability has included some studies which resulted in the localization of the gene for the enzyme paraoxonase, which plays a key role in the metabolism of these compounds. In addition, scientists have mapped the occurrence of this enzyme's activity in families. This work gained major significance with the recent discovery that the gene for this paraoxonase enzyme is located close to a gene which is apparently responsible for cystic fibrosis, and is a readily identifiable marker for that disease's gene.

- NIGMS research support has aided the development of prototypes for artificial red blood cells. Such artificial red blood cells might prove useful for expanding blood volume after injury or trauma, and for substituting temporarily for natural red blood cells until a more appropriate transfusion becomes available. These artificial red blood cell prototypes, known as neohemocytes, appear to be capable of transporting oxygen to tissues and releasing it where it is needed. In preliminary experiments, replacement of 95 percent of the blood of rats with a suspension of neohemocytes has led to the survival of these animals for 18 hours or more. Furthermore, the small size of these artificial red blood cells, compared to normal red blood cells, makes them especially valuable for transporting oxygen to those oxygen-deficient tissues served by blood vessels that have been partially blocked or constricted by disease or injury.

- Malignant hyperthermia, a genetically determined reaction to anesthesia in which there is often a fatal rise in body temperature and a disordering of normal metabolic function, has been found to be due, in part, to a defect in the ability of muscle cells to control the release of intracellular calcium during contraction. This finding was made possible because of the availability of an animal model, a breed of pig susceptible to malignant hyperthermia, and should provide the basis not only for improved therapy, but also for the eventual identification of the gene responsible for this disorder.

Support under this program is provided through the use of investigator-initiated research grants, research center grants, research contracts, and both individual and institutional fellowship awards.

Rationale for the Budget Request

The 1987 request of $70,147,000 for Pharmacological Sciences represents a increase of $189,000 over the 1986 revised estimate. This request will provide for 461 research project grants, 3 research centers, 4 other research awards, and 280 trainees.

The Pharmacological Sciences Program will support research in a number of promising areas in 1987, among them:

1. Drug Metabolism: For many years, researchers have been studying key enzymes (large protein molecules that "speed up" biochemical reactions) that are involved in the metabolism of drugs in the liver and other organs. Only recently, however, have scientists been able to develop dramatic new insights

into the way in which the levels of these enzymes are controlled. By utilizing the techniques of recombinant DNA technology and molecular biology, investigators have begun to clarify the relationships among a group of enzymes known as the monooxygenase or P450 enzymes. There are at least a dozen forms of the P450 enzymes, many of which occur in diverse species such as plants, bacteria, and insects. Understanding the underlying molecular events that control the levels of the P450 enzymes is important because the P450 system is responsible for metabolizing drugs, hormones, and toxic substances -- many of which are carcinogenic -- found in the environment. Therefore, broadening our knowledge of the regulation of the P450 system will not only help scientists better understand how humans respond to the insults presented by foreign compounds, but will also help researchers understand how insects and bacteria develop resistance to the insecticides and antibiotics that have been devised for the control of insect infestation and bacterial disease, respectively.

Related work in drug metabolism has also allowed investigators to understand the variability -- often genetically based -- in people's response to drugs. For instance, scientists have discovered that the Japanese metabolize the anticonvulsant drug, mephenytoin, more slowly than do otherwise similar Caucasian populations. This results in higher blood levels of active drug which last for longer periods, requiring downward adjustment of dose. Given the fact that pharmaceutical companies frequently test new drugs in selected populations around the world but ultimately market those drugs worldwide among many different racial or ethnic populations, there is a profound need for further research into such variability in drug metabolism. This research should lead to the development of newer and safer drugs, as well as to the protection of specific subpopulations from potential side effects of those drugs currently in use.

2. Antibiotic and Antitumor "Killer Probes": Many antitumor and antibiotic agents function by interfering with the structure or metabolism of DNA, the basic genetic material, of the bacteria, viruses, or tumor cells which they are supposed to inhibit or kill. A problem that has faced scientists and clinicians is that many drugs which are toxic to infectious agents or tumor cells also affect normal cells. A promising new approach being developed by some investigators is the design of very specific "killer probes." In studies on viral infections, these killer probes consist of nucleotide sequences that are complementary to unique sequences found in viral messenger RNA. The probes combine specifically with these complementary sequences, thereby inhibiting synthesis of viral proteins, and thus of the whole virus, the disease agent. An exciting innovation to this approach that currently is under study is the placement of chemical components on the nucleic acid probe which can react in such a way with the viral messenger RNA that inhibition of the production of viral proteins is more long-lasting, perhaps even permanent.

3. G-proteins: Cells respond to drugs (as well as to hormones and neurotransmitters) via a two-step process. The drug first binds to receptors on the cell surface. This drug-receptor complex acts as an extracellular signal which is converted to an intracellular signal called cyclic AMP. There is a family of membrane-bound proteins (termed G-proteins) which bind the compound GTP (guanosine triphosphate) and act as integral parts of this information transfer system. Much work has been done to understand the functioning of this family of G-proteins. The gene for the G-protein which

stimulates cyclic AMP formation has been cloned. It has been shown that in those mutant cells which fail to transfer signals from the receptor to the cyclic AMP, there is a deficiency or total absence of the G-protein and of the messenger RNA which codes for it. A clinical manifestation of this condition is the disorder known as pseudohypoparathyroidism. Another member of this G-protein family is the protein transducin, which is necessary for vision. The transducin gene has also been cloned and compared with other members of the G-protein gene family.

These studies have shown that the entire family of G-proteins shares common amino acid sequences in all of their subunits, implying that they were all coded for by some common genetic precursor at some point in the distant past. Some have evolved as integral components of everyday cellular processes, while others with similar functions appear to operate only in abnormal states such as cancer. Understanding the general way in which the G-proteins function may lead to increased insight into the mechanism whereby normal cells become tumor cells, as well as into other diseases known to involve some as-yet-undefined defects in progression of the neurotransmitter-receptor-information transfer process (e.g., Alzheimer's disease, Parkinson's disease).

4. Plant Biochemistry: A primary pathway in both plants and microorganisms for making vitamins, growth promoters, and a variety of hormones is the "shikimic acid pathway." One vitamin made by this route is vitamin K, an essential component of the synthesis of blood-clotting factors by the liver in man. The biosynthesis of this vitamin has recently been clarified and the intermediate compounds and steps in the synthesis identified. By studying the various enzymes and reaction sequences involved in each step of the shikimic acid pathway, investigators can develop methods for the test-tube synthesis of the resultant vitamins and hormones.

Many of the early enzymatic steps in the shikimic acid pathway have been elucidated in plants. Such work will help microbiologists better define the role that this pathway plays in microbial growth, which will lead to more effective ways of regulating microbial growth in culture for many biotechnology applications. Isolation and characterization of these natural products can be expected to lead to novel methods for the test-tube synthesis of vitamins, hormones, and growth factors which are currently available only in small quantities and at high cost from natural sources. Knowledge of the mechanisms by which these compounds are synthesized should also lead to the design of both inhibitors and stimulators of microbial growth to benefit both agriculture and biomedical science. For example, certain similarities have been found between the growth factors in plants which induce plant tumors via DNA transfer, and some mammalian oncogene products. Understanding the role of these growth factors and the ability of plant hormones to suppress them may also contribute to an increased understanding of the cancer process in man.

5. Anesthesiology: Much of the risk that occurs when an individual undergoes surgery actually is due to the reaction to the anesthesia. Efforts to minimize this risk are complicated because of individual variations in the reactions to anesthetic agents, due to age, genetic differences, other drugs that a patient might be receiving or have received in the recent past, or the patient's physical condition. Physical conditions that are now known to affect one's response to anesthesia include altered kidney, liver, or lung

function, and extensive burns. Furthermore, specific anesthetic agents may alter certain physiological responses, thus introducing risks for patients being treated for certain diseases or injuries, such as victims of head injury who are being treated for elevated intracranial pressure. Research supported by the PS Program that will provide information concerning the factors that affect individual responses to anesthetic reagents, or that will identify the safest anesthetics for specific circumstances, are of clear clinical importance.

Pharmacological Sciences

Impact Data	1986 Appropriation	1986 Available after Sequestering	1986 Revised Estimate	1987 Estimate
Res. proj. grants				
Number	481	481	454	461
Amount	$66,235,000	$63,153,000	$62,054,000	$63,000,000
Res. centers				
Number	4	4	4	3
Amount	2,340,000	2,340,000	2,340,000	1,735,000
Other res.				
Number	9	9	9	4
Amount	286,000	286,000	286,000	160,000
Training				
FTTP	324	311	311	280
Amount	5,505,000	5,278,000	5,278,000	5,252,000
Total	74,366,000	71,057,000	69,958,000	70,147,000

National Institute of General Medical Sciences

Biophysics and Physiological Sciences

1987 Authorization: Indefinite.

Obligational Authority:

1986 Appropriation	1986 Available after sequestering	1986 Revised Estimate	1987	Increase or decrease
$101,263,000	$96,167,000	$94,870,000	$94,774,000	-$96,000

Purpose and Method of Operation

The Biophysics and Physiological Sciences (BPS) Program supports basic biomedical research studies directed toward three primary goals: (1) gaining a better understanding of the structures and functions of biologically important molecules, such as proteins, through the use of theories and tools common to physics; (2) the development of new methods and instrumentation for use in molecular and cellular analyses; and (3) gaining an in-depth knowledge of the physiological effects of severe burns and other forms of trauma on the body, with an eye toward developing information useful to the clinical care of individuals suffering from such trauma.

Biophysics

The BPS Program was established just one year ago, by the expansion of the existing Physiology and Biomedical Engineering Program to include aspects of biophysics previously distributed through other programs within the Institute. Central to the rationale for this reorganization was the rapid growth in recent years of research opportunities in the biophysical sciences field, and the consequent need to provide a central focus within the NIGMS for such research.

It has long been recognized that the development of new technologies and instrumentation makes new types of investigations possible, while creating new opportunities in even well-established fields. But, perhaps even more than in most areas of biology, advances in biophysics have been closely linked to advances in technology. Illustrative is the case of X-ray crystallography, the development and refinement of which are allowing scientists to determine the precise three-dimensional structure of such important biological substances as myoglobin, an iron-containing pigment found in skeletal muscle, especially in muscles which must remain in sustained contraction. Information of this kind is critical to obtaining a clear understanding of the way in which myoglobin and other similar substances work, as well as to determining what happens when structural abnormalities occur. For example, some scientists have suggested that defects in the structure of myoglobin molecules may be related to Duchenne's muscular dystrophy, a disorder characterized by severe muscular paralysis; and while the evidence for this has now been disputed, it is nevertheless clear that there is a link between this disease and abnormally low levels of myoglobin. Investigators are now convinced that the ability to identify the nature of structural abnormalities which exist at the molecular level (e.g., in proteins) will represent a critical step in the battle against diseases, because it will allow effective therapies to be developed.

The causative agents of the common cold are now also targets of such structural analysis. Using biophysical tools developed with NIGMS support, Dr. Michael Rossman of Purdue University (whose molecular structure studies were supported by the NIGMS over a period of many years) recently determined the three-dimensional structure of one type of human cold virus — the first time that any animal virus has been successfully described in detail. This breakthrough is significant because it should enable investigators to study the structural features of these viruses in depth, identifying in the process the specific sites at which they attach to and then enter cells to cause infections. This knowledge, in time, should allow scientists to develop better methods for fighting such infections.

In addition to X-ray crystallography, which is clearly among the most important tools of the biophysicist, biophysics researchers have developed a series of other instruments which have dramatically expanded their abilities to measure and study biological objects — the best known being nuclear magnetic resonance (NMR) spectroscopy. NMR is an important technique because it allows substances to be studied in their natural, as opposed to an artificially created, crystalline, state. Currently, however, much of the progress being made in the development of instrumentation is attributable to the recent availability of moderately priced computers and a trend toward combining several instruments and techniques to achieve greater analytical capabilities than any single instrument can provide. For example, a technique called "fluorescent imaging" combines the use of lasers with fluorogenic substrates. This new approach has helped to overcome a number of previously existing problems — allowing, for example, the visualization of particular cellular components despite the presence of a large excess of other materials, which tend to hide the components being studied.

The development of new laboratory instrumentation and techniques is an important goal of the BPS Program.

Physiological Sciences

Trauma, including burn injury, is the leading cause of death among people 1 to 44 years of age and the fourth leading cause of death in all age groups. Burn injury, which is a special form of trauma, hospitalizes 75,000 people each year. One-third of these burn victims are children under age 15. Approximately 12,000 burn victims die annually, making burn injury the third leading cause of accidental death in the United States.

In the immediate 24-hour period after extensive trauma or severe burn injury, a cascade of systemic responses occurs. When these changes are prolonged, they often culminate in respiratory and cardiovascular collapse, metabolic dysfunction, kidney failure, and overwhelming infection, any of which may lead to death. Among surviving patients, scarring and distortions of skin and muscle tissue, called contractures, can result in major disfigurement and physical disabilities, accompanied by severe psychological stress and the need for extensive rehabilitation.

The major problem facing scientists in the field of trauma and burn research is the absence of an adequate understanding of the mechanisms that underlie the complications of severe injury, including burns. Much more needs to be known about the basic molecular, biochemical, and physiologic changes caused by this type of injury. Through the BPS Program, the NIGMS supports research designed to elucidate: (1) the role of fibronectin and other naturally produced proteins in the abnormal changes caused by shock and trauma; (2) the nature of wound healing and the effect of growth substances on such processes; and (3) the immunologic and physiologic alterations which occur following burn injury. A major development in this area, and one still being worked on by NIGMS grantees, has been the evolution of an artificial skin to reduce scarring, eliminate infections, and speed healing following serious burn injury.

During the past year, important discoveries were made by grantees of the BPS Program in the following areas:

° Using X-ray crystallographic methods, investigators at Yale University have determined a "low resolution" structure for resolvase, an enzyme which plays a significant role in a number of important genetic processes, including gene transcription and recombination.

° Researchers at the University of Washington succeeded in the development of a technique for two-dimensional nuclear magnetic resonance (NMR) spectroscopy to directly study the mechanisms by which gene expression (the triggering of protein production) is controlled at the level of molecular, and even atomic, detail. Research by investigators in the same laboratory led to the development of a method to delineate the three-dimensional structures of nucleic acids and proteins directly from solution, combining two-dimensional NMR data with computer analysis. The progress made by these grantees suggests an increasingly important role for NMR in studies of the molecular structure of biological polymers, with a level of precision perhaps rivaling X-ray crystallography, but without the sometimes frustrating requirement of growing crystals.

° Researchers at Princeton University have elucidated the physical properties of the lipid molecules which are one constituent of retinal cell membranes in vertebrates, helping to explain the biomechanical "interplay" which occurs between lipid composition and structure in the cell membranes of the retina (the light-focusing area of the eye). This study involved the combined use of X-ray diffraction, NMR, and electron microscopy techniques.

° Researchers at the New York University Medical Center have developed new imaging techniques which will allow the three-dimensional structure of actin, an important muscle protein, to be more clearly delineated. Their efforts are expected to lead to a more complete understanding of how actin works with other proteins to allow muscle contraction.

- Burn researchers at the University of Michigan at Ann Arbor have discovered a possible cause for the secondary lung damage which often follows burns; in addition, they have discovered that treatment with an enzyme called catalase can significantly reduce lung damage after thermal injury.

- Investigators at the University of Texas Health Science Center have developed a composite skin graft for burn treatment which significantly aided wound healing in test patients, with little or no development of contractures and minimal scarring.

Support under this program is provided through the use of investigator-initiated research grants, research center grants, R & D contracts, and both individual and institutional fellowship awards.

Rationale for the Budget Request

The 1987 request of $94,774,000 for Biophysics and Physiological Sciences Program represents a decrease of $96,000 from the 1986 revised estimate. This request will provide for 552 research project grants, 5 research centers, 6 other research awards, and 777 trainees.

The BPS Program will provide special emphasis to the following areas in 1987:

1. Crystallographic Studies: Among the methods for determining molecular structure, X-ray crystallography remains paramount. This fact was highlighted during the past year with the presentation of the 1985 Nobel Prize in chemistry to a former NIGMS grantee, Dr. Herbert Hauptman of the State University of New York at Buffalo, for his development of statistical procedures which have served to successfully speed up the process by which X-ray crystallography is used to delineate the structure of molecules. While Dr. Hauptman's work was initially concentrated on the analysis of very small molecules (100 atoms or less), his recent work focuses on the extension of these methods to the study of large biological molecules, such as proteins. If he and others working in this field are successful, it is possible that the structure of a wide range of biological molecules will be understood, and that many biological functions could eventually be defined in very precise structural mechanical terms. Research concerned with improvements in the technology and methodology of X-ray crystallography will be given a very high priority within the BPS Program in 1987, with emphasis also being placed on the application of crystallographic studies to the analysis of lipids and protein-nucleic acid interactions.

2. NMR Studies: New developments in the use of nuclear magnetic resonance show considerable promise in being able to help determine molecular structures in aqueous solution at an atomic level of resolution. This has been shown through studies of both nucleic acids and proteins. Particularly impressive has been the ability of NMR to elucidate internal movement within proteins — something which such static methods as X-ray crystallography are not able to accomplish. Continued support will be provided for efforts to expand the uses of NMR in structural studies over the next year.

3. Raman Spectroscopy: Raman spectroscopy makes use of scattered light to determine the "vibrational (energy) bands" of a molecule, allowing molecules, such as proteins, to be differentiated on the basis of a kind of light-scattering "fingerprinting" technique. Although C.K. Raman, an Indian scientist, discovered the Raman effect in the 1920's — a discovery for which he received the Nobel Prize in 1930 — the use of Raman spectroscopy to study biological systems is still relatively new. This technique remained almost dormant for 50 years, due to the lack of a suitably intense monochromatic light source. This situation has changed, however, with the advent of lasers, as well as the discovery of a mechanism for enhancing the Raman effect by "exciting" the molecules being studied. Recently, two NIGMS grantees developed a technique, utilizing newly developed pulsed lasers, to excite proteins and nucleic acids in the ultraviolet region of the light spectrum, making Raman spectroscopy even more useful and opening up an important new approach to the study of "protein folding" and other structural characteristics of molecules which affect their activity.

4. Burn and Trauma Research: Infection, shock, and lung damage remain major complications and causes of death in seriously burned patients. Consequently, research on the immunologic and physiologic alterations which occur following burn injury is of intense interest. In recent years, many of these potentially fatal complications have been shown to be linked to the release in the body of powerful "mediators," substances which are actively involved in the tissue damage which occurs, particularly in the lungs, of burn victims. Studies aimed at understanding how such mediators are released and how they work will be a very high priority of the BPS Program in 1987. Such information is considered prerequisite to the development of protocols for the effective control of inflammatory responses.

A second area of emphasis will be the further development of an artificial skin for use in the treatment of burn injuries. Following a severe and extensive burn, one of the primary needs is to quickly replace the skin in order to avoid infection, prevent fluid loss, and retain body heat. These are life-threatening problems that must be dealt with quickly, preferably in a matter of days. In the case of very extensive burns, the time-honored practice of grafting the patient's own skin onto the wounds cannot be followed since an insufficient amount of unburned skin is available. NIGMS grantees have had considerable success in the development of artificial skin substitutes for grafting, and continued support will be provided by the BPS Program for efforts in this area.

Biophysics and Physiological Sciences

Impact Data	1986 Appropriation	1986 Available after Sequestering	1986 Revised Estimate	1987 Estimate
Res. proj. grants				
Number	592	592	548	552
Amount	$78,172,000	$74,544,000	$73,247,000	$73,947,000
Res. centers				
Number	8	7	7	5
Amount	4,177,000	3,738,000	3,738,000	2,404,000
Other res.				
Number	10	9	9	6
Amount	1,974,000	1,712,000	1,712,000	1,946,000
Training				
FTTP	897	857	857	777
Amount	16,940,000	16,173,000	16,173,000	16,477,000
Total	101,263,000	96,167,000	94,870,000	94,774,000

National Institute of General Medical Sciences

Minority Access to Research Careers

1987 Authorization: Indefinite.

Obligation Authority:

1986 Appropriation	1986 Available after sequestering	1986 Revised Estimate	1987	Increase or decrease
$7,950,000	$7,950,000	$7,950,000	$7,066,000	-$884

Purpose and Method of Operation

The continued underrepresentation of blacks and other minority groups in scientific fields underscores the fact that the United States is still witnessing a significant loss of potential talent from important segments of our society. According to data from the Ford Foundation, minorities constitute more than 20 percent of the nation's college age population, but they accounted for only 8 percent of the Ph.D.s awarded in 1983. Blacks, Puerto Ricans, Mexican Americans, and American Indians together accounted for only 4.4 percent of this total. The problem is even more serious in the biological sciences. A survey by the National Research Council found that blacks received only 2.4 percent of the biomedical science doctoral degrees awarded in 1982. U.S. Department of Education statistics indicate that in 1982 blacks and Hispanics together comprised only 4.5 percent of full-time graduate students in the biological sciences, and in 1981 members of these two groups received only 9.6 percent of all bachelor's degrees awarded in the biological sciences.

It is evident that minority group members are underrepresented at all stages of schooling and scientific careers, but that the disparity widens considerably after the receipt of a bachelor's degree. A recent study by the Institute of Medicine of the National Academy of Sciences found that three factors are primarily responsible for the increasing disparity as students move from undergraduate to graduate education: differences in the structure of opportunities; differences in student aspirations; and differences in student preparation. With regard to opportunities, minority students often do not benefit from the institutional reputations of the schools they have attended or the kinds of networks available to students in major research institutions. With regard to aspirations, a lack of information and encouragement and a shortage of role models may work against the aspirations of the minority student. With regard to preparation, minority students may not receive the same degree of laboratory exposure, research experience, and faculty supervision that majority students tend to receive.

In an effort to address these issues — opportunity, aspiration, and preparation — in 1975 the NIGMS established the Minority Access to Research Careers (MARC) Program. This Program provides special research training opportunities and incentives in the biomedical sciences to attract and retain minority students with research career potential. Four mechanisms are used to implement this Program. These are: (1) the MARC Honors Undergraduate Research Training Program; (2) the MARC Predoctoral Fellowship Award; (3) the MARC Faculty Fellowship Program; and (4) the MARC Visiting Scientist Award.

The MARC Honors Undergraduate Research Training Program was established in 1977 at the suggestion of the Congress, based on recommendations of Institute consultants and staff. It emphasizes the value and importance of providing biomedical research training at the undergraduate level in minority institutions. Its objectives are to help minority institutions develop strong undergraduate science curricula, to stimulate an interest in undergraduate research, and to increase the number of well-prepared minority students who can compete successfully for entry into graduate programs leading to the Ph.D. degree in the biomedical sciences. Under this program, highly qualified minority institutions receive support to teach and provide research training for honors undergraduates who are in their third or fourth year of college, and who plan to obtain the doctorate degree (Ph.D.) in an area of biomedical science. Fifty-four minority institutions around the country have received support under this program. At these institutions there are now approximately 50 percent more science majors than there were prior to the receipt of NIGMS support.

Eligible students are selected on the basis of both their academic achievements and their commitment to seek graduate training. In 1985, the Honors Undergraduate program had a total of 192 graduates, bringing the total number of graduates since 1978 to almost 850. To date, approximately 80 percent of these graduates have gone on to either graduate or professional schools. It is hoped that this program will result in a progressive increase in the pool of qualified minority scientists who are available to compete successfully for research grants and to serve as mentors and role models for new generations of minority biomedical investigators.

The MARC Predoctoral Fellowship Award provides support for outstanding graduates of the MARC Honors Undergraduate Program to pursue doctoral degrees in the biological sciences. Established in 1982, this relatively new award mechanism gives a further incentive to graduates of the Honors Undergraduate Program to obtain research training in the nation's best graduate programs. Awards are conditional upon acceptance into an approved doctoral (Ph.D.) degree or combined degree (M.D.-Ph.D.) program in the biomedical sciences. To date, 138 applications for this award mechanism have been received, and 59 have been funded. The relatively low number of applications may be an indication that significant numbers of MARC Honors graduates are successfully entering the educational mainstream and securing their own predoctoral funding from graduate schools anxious to recruit them.

The MARC Faculty Fellowship Program provides opportunities for advanced research training to selected faculty members of four-year colleges, universities, and health professional schools in which student enrollments are drawn substantially from minority groups. These institutions may nominate faculty members for MARC Fellowships in support of a period of advanced study and research training in graduate departments and laboratories, either as candidates for the Ph.D. degree or as investigators obtaining postdoctoral research training in the biomedical sciences. When the period of training is completed, fellows are expected to return to their sponsoring schools to do research and teaching. Since its inception in 1972, 193 individuals have received support under this program. Of those who have completed their training period, approximately 84 percent have returned either to their original home institution or to another minority institution. The research training sites have included 70 universities, research laboratories, and federal institutions in 32 states and 5 foreign countries. The home institutions also are broadly representative, including 68 universities in 23 states and the Commonwealth of Puerto Rico.

The MARC Visiting Scientist Award provides support for outstanding scientist-teachers to serve in the capacity of visiting scientists at four-year colleges, universities, and health professional schools in which student enrollments are drawn substantially from minority groups. The primary intent is to strengthen research and teaching programs in the biomedical sciences for the benefit of students and faculty at these institutions, by drawing upon the special talents of scientists from other, primarily majority, institutions. Reciprocal benefits also should accrue to the Visiting Scientist through the added experience gained by involvement in innovative science education and research development programs. The program includes detailed arrangements for the Visiting Scientist to reside in the campus community and to participate fully in programs of teaching, development of research, and counseling. This necessitates considerable advance planning on the part of both the host institution and the prospective visiting scientist. As a result, only 16 applications have been received and nine awards made since the inception of this award mechanism. However, concerted staff efforts to advertise and encourage applications are being made, and both the MARC Review Committee and the National Advisory General Medical Sciences Council strongly support continuation of this award mechanism.

In addition to the above, the MARC Program has sought to provide advice and technical assistance to minority students, colleges, and universities wherever possible, and to encourage discussion regarding the obstacles which continue to hold the number of minority scientists in the country to a relatively low level. In 1985, for example, the NIGMS sponsored the fifth MARC Undergraduate Scholars Conference, at which MARC-supported college seniors gave poster presentations about their research projects and met with graduate school faculty and scientists at the NIH to discuss existing opportunities in graduate education and research.

Rationale for the Budget Request

The 1987 request of $7,066,000 for Minority Access to Research Careers Program represents a decrease of $884,000 from the 1986 revised estimate. This request will provide for 395 trainees.

As in previous years, the MARC Program will continue to place primary emphasis on its Honors Undergraduate Research Training (HURT) component in FY 1987, with roughly 80 percent of the MARC budget being allocated to this component. The recent Institute of Medicine study found that, of former MARC undergraduate trainees no longer in school, 62 percent are employed in science or engineering fields. This was above the levels found in the most closely comparable national data. Another indication of success is the high level of demand for MARC trainees. At the annual MARC Scholars Conferences, for example, HURT trainees have been recruited by dozens of major research universities. MARC program directors also report that they are frequently approached with inquiries from graduate schools about their trainees and that research laboratories throughout the country have provided opportunities for short-term research training experiences to HURT trainees.

The "honors" concept of the MARC Program has encouraged institutions that are recipients of awards to establish a different and more rigorous program for students in the basic sciences. Many have incorporated an honors thesis requirement for graduating MARC students. The provision of funds for seminars and lectures, release time for faculty members, up-to-date equipment and supplies, as well as the addition of full-time and part-time faculty in disciplines not formerly represented, have all contributed to academic enrichment. In addition, specialized courses have been set up to prepare students to take standardized tests — an area in which minority students traditionally have been weak. The scientific activities of grantee departments have been strengthened and, as a result, it has become more common for MARC faculty members and trainees to be invited to present papers at local, regional, and national scientific meetings. We are also beginning to see a larger number of students serving as coauthors of scientific papers. In summary, the MARC Program, and especially its HURT component, has produced a new awareness among minorities of the opportunities available in biomedical research, and has provided the means to take advantage of these opportunities.

Minority Access to Research Careers

Impact Data	1986 Appropriation	1986 Available after Sequestering	1986 Revised Estimate	1987 Estimate
Training				
FTTP	478	478	478	395
Amount	$7,950,000	$7,950,000	$7,950,000	$7,066,000
Total	7,950,000	7,950,000	7,950,000	7,066,000

National Institute of General Medical Sciences

Intramural Research

1987 Authorization: Indefinite.

Obligational Authority:

1986 Appropriation	1986 Available after sequestering	1986 Revised Estimate	1987	Increase or decrease
$875,000	$837,000	$837,000	$875,000	+$38,000
		(FTEs: 21)	(21)	(—)

Purpose and Method of Operation

The NIGMS has a small, but unique intramural research program formally known as the Pharmacology Research Associate Training (PRAT) Program. Under its auspices, a group of young scientists are selected each year for a two-year period of postdoctoral research under the tutelage of preceptors in the laboratories of the various categorical institutes of the National Institutes of Health and the Alcohol, Drug Abuse, and Mental Health Administration. In FY 1985, 22 first- and second-year PRAT fellows worked in 15 different laboratories in seven different institutes. The goal of this program is to develop topflight leaders in pharmacological research who will take key positions in academic, industrial, and governmental research laboratories. The program is intended for those who have made a commitment to pharmacology through their training or research, and for those with backgrounds in clinical medicine or basic science who wish to acquire specialized experience in the field of pharmacology.

The PRAT Program was established in 1965, and in the 20 years of its existence, 189 scientists have graduated from the Program. Of these, it is known that at least 172 (91 percent) have entered research careers. Of those employed in research, 81 are located at academic or independent research institutions, 70 at NIH or other Federal research facilities, and 20 at various pharmaceutical firms. Over 40 percent of the PRAT graduates engaged in research possess an M.D. degree, indicating that the program has attracted a large number of physicians and directed them into research careers instead of into clinical practice.

The young men and women chosen for this program are selected on the basis of their academic records, demonstrated research interests, and research accomplishments. They receive high-quality postdoctoral research experience under the direction of one of more than 94 senior scientists, including Nobel Prize winners Drs. Julius Axelrod and Marshall Nirenberg. In addition, they may take coursework in such areas as pharmacokinetics, experimental statistics, medicinal chemistry, human biochemical genetics, and molecular biophysics.

All of these factors have combined to make the PRAT Program widely recognized for its excellence. Over the years, the Program has produced many leaders in pharmacological research, and its most recent graduates continue to be involved in innovative research having great potential for solving problems of pharmacologic interest. Indeed, in the last 12 years, four former PRAT fellows have won the J.J. Abel Award, the most prestigious award given to young investigators by the American Society for Pharmacology and Experimental Therapeutics.

Since 1978, the PRAT Program has made several positions available which are specifically targeted to the area of clinical pharmacology. Applicants for such positions must have the M.D. degree, a minimum of 1 year of graduate medical training (internship, residency), and a demonstrated interest in a research career in clinical pharmacology. This sub-program offers qualified candidates opportunities for training in research directly related to the distribution, mode of action, metabolism, and excretion of drugs in the human body, and is designed to attract more physicians into what is considered to be a shortage area. There are estimated to be fewer than 100 clinical research pharmacologists in the entire country.

Rationale for the Budget Request

The 1987 request of $875,000 for the NIGMS Intramural Research Program represents an increase of $38,000 from the 1986 revised estimate. This request will provide support for a total of 21 PRAT fellows, the same as in 1986.

National Institute of General Medical Sciences

Research Management and Support

1987 Authorization: Indefinite.

Obligational Authority:

1986 Appropriation	1986 Available after sequestering	1986 Revised Estimate	1987	Increase or decrease
$13,299,000	$12,726,000	$12,726,000 (FTEs: 139)	$13,299,000 (139)	+$573,000 (—)

Purpose and Method of Operation

This activity provides funds for salaries, travel, and other administrative costs associated with the professional and support staff of the Institute. In 1987, the Office of the Director will continue to provide the professional leadership and guidance needed to manage NIGMS programs. This Office evaluates research needs and selects promising research areas for new or expanded investigation. The Office also maintains contact with the scientific community and the public through the regular dissemination of information pertinent to their concerns.

The staff in the various program areas will provide the scientific direction and administrative support required for the approximately 3,197 grants and 5 research and development contracts to be funded by NIGMS in 1987. Staff members will manage grant-supported programs; coordinate peer review of competing grant applications for scientific merit and program relevance; serve as contacts for investigators, applicants, grantees, advisory groups, and other components of the NIH, PHS, and other organizations; and compile and report scientific and fiscal information relevant to grant programs.

This activity also supports: (1) services provided centrally by NIH organizational units which do not receive direct appropriations, such as the Division of Research Grants; (2) program evaluation studies; and (3) the National Advisory General Medical Sciences Council.

Rationale for the Budget Request

The 1987 budget request of $13,299,000 for Research Management and Support represents an increase of $573,000 over the 1986 revised estimate.

During 1987, continued emphasis will be placed on management reforms and the streamlining of administrative procedures in order to more effectively carry out the Institute's mission.

National Institute of General Medical Sciences

Detail of Permanent Positions

	1985 Actual	1986 Estimate	1987 Estimate
ES-5	1	1	1
ES-4	3	3	3
ES-1	1	2	2
Subtotal	5	6	6
GS/GM-15	9	11	11
GS/GM-14	19	17	17
GS/GM-13	11	12	12
GS-12	16	15	15
GS-11	22	23	23
GS-9	6	5	5
GS-8	8	8	8
GS-7	28	30	30
GS-6	13	10	10
GS-5	8	10	10
GS-4	12	10	10
GS-3	6	6	6
Subtotal	158	157	157
Grades established by Act of July 1, 1944, (42 U.S.C. 207):			
Director Grade			
Senior Grade	2	2	2
Subtotal	2	2	2
Total permanent positions	165	165	165

MONDAY, MARCH 17, 1986.

DIVISION OF RESEARCH RESOURCES

WITNESSES

BETTY H. PICKETT, DIRECTOR
JAMES B. WYNGAARDEN, DIRECTOR, NIH
JAMES F. O'DONNELL, DEPUTY DIRECTOR, DRR
RICHARD L. SHAFER, EXECUTIVE OFFICER, DRR
WILLIAM K. RUSS, BUDGET OFFICER
DENNIS P. WILLIAMS, ACTING DEPUTY ASSISTANT SECRETARY, BUDGET, DHHS

Mr. NATCHER. We take up next the Division of Research Resources.

We have before the committee Dr. Betty H. Pickett, Director of the Division of Research Resources, and it is a pleasure to have you back before the committee.

Before you give us your statement, tell us who you have with you at the table.

Dr. PICKETT. I have with me the Deputy Director of our Division, Dr. James O'Donnell and next to him Mr. William Russ, Budget Officer of the Division and next to him Richard Shafer, the Executive Officer of the Division.

Mr. NATCHER. We are delighted to have all of you before the committee at this time, and we will be pleased to hear from you.

OPENING STATEMENT

Dr. PICKETT. I am pleased to appear before you again.

Through the Division of Research Resources, NIH provides facilities, instruments, and technologies, experimental animals and other key resources that are utilized by more than 18,000 researchers supported by more than 5000 grants worth close to $800 million.

Through the Clinical Research Program, scientists have access to 600 research beds, outpatient facilities, core laboratories and diet kitchens for studies related to a host of diseases and conditions such as, among others, AIDS, diabetes, cancer, metabolic problems, genetic diseases, problems of aging, neonatology, et cetera. The 78 centers provide 87 percent of the capacity for NIH-supported patient-oriented research, including some of the major clinical trials supported by the NIH Institutes.

In 1985, we updated and expanded the data management system and are now linking all the centers into an electronic mail network to facilitate coordination among them.

The Biomedical Research Technology Program makes available major instrument facilities and technologies at locations around the country, including computer and bioengineering resources, centers for imaging and for analysis of biological materials in the most intimate detail of molecular structure and function.

1985 funds enabled significant expansion in Nuclear Magnetic Resonance, both for basic and clinical studies; at one center, a very high resolution new system is under development; also a new laser resource at MIT to develop medical applications; a new electron microscope facility to develop new image analysis methods for intermediate voltage transmission instruments to develop technology for specimen preparation afore the new technology.

Supercomputer access for biomedical researchers supported by NIH grants is another new area: we will begin providing orientation to these computer systems and machine time as well, in cooperation with NSF.

DRR's Animal Resources Program—we have been upgrading facilities in the primate research centers which maintain colonies of 14,000 subhuman primates of numerous species along with facilities to study them and the necessary skilled staff: areas of study include neurosciences, immunology, reproductive biology, aging, vision, hearing, fetal development and many others.

The diagnostic labs focus on health and diseases of lab animals such as the rat, mouse, rabbit, etc in order to provide the healthiest animals for research. Our new program of renovation of lab animal facilities was initiated in 1985 with 23 awards that will help institutions meet the tightened requirements of both the *NIH Guide to The Care and Use of Laboratory Animals* and the new NIH/PHS animal welfare policy.

The Shared Instrument Grant Program has by now provided close to $100 million and nearly 550 sophisticated scientific instruments for biomedical research; these can be shared by groups of PHS-funded researchers who need to update or replace worn out or obsolete lab equipment: EM's, NMR's, spectrometers, cell sorters, fermentors and other items for the new biology are in great demand.

The formula or BRS Grant this year will provide $59.5 million to 575 medical, dental, nursing, pharmacy and other health professional and graduate schools, research hospitals and institutions for flexible use by thousands of investigators, locally determined. Most popular uses continue to be for pilot, emergency, interim needs, and central resources.

The high school summer research apprentice program for minority high school students continues, with 1000 placed in biomedical research labs in close to 300 universities and colleges: last year four of these students received honors in the Westinghouse Science Talent Search.

The Minority Biomedical Research Support Program, now fourteen years old, is developing a key human resource. It provides institutions heavily serving minorities support for some 1500 students and 800 faculty via 92 grants for the conduct of around 650 subprojects and for renovation needs and equipment upgrade and replacement.

Recent preliminary data indicate doctoral degrees awarded to over 900 former MBRS students so far, in the sciences, medicine and dentistry, with several hundred more still in training. Both students and faculty continue to increase their participation in scientific meetings and publication.

Our 1987 budget request shows most DRR programs with only small changes, plus or minus from the 1986 revised level. One element is completely eliminated—the Biomedical Research Support or formula grant.

Our request for 1987 is $234,192,000. A reduction of $56.5 million or 19.5 percent below the revised 1986 request.

I shall be pleased to respond to your questions.

[The statement of Dr. Pickett follows:]

DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health
Statement of the Director
Division of Research Resources

I am pleased to present the 1987 budget request for the Division of Research Resources (DRR).

The Division provides for the development, support, and administration of research resources which complement and augment NIH's extramural research project grant, research contract and research training activities by operating five distinct programs.

The Clinical Research Program continues to provide specialized environments and resources necessary for the conduct of high quality clinical research through a nationwide program of General Clinical Research Centers. Seventy-six Centers will be supported in 1987. Research advances include important discoveries in relation to glaucoma, high blood pressure, diabetes, cancer, and multiple sclerosis (MS). For example, a synthetic substance called Copolymer I reduces the number of attacks of MS and arrests the progression of disability. New studies now show that an insulin-containing nasal spray may be an important adjunct to injections for insulin delivery. Eighteen General Clinical Research Centers supported work on AIDS, including studies of opportunistic infections in immunocompromised patients, epidemiological studies of AIDS patients, and therapeutic interventions for both the primary disease and secondary infections.

The Centers provide an outstanding environment for the research training of young physicians through the Clinical Associate Physician (CAP) appointments. Forty-seven were appointed in 1985. Overall, 130 young physicians have served as CAPs since 1974; all but 14 remain in academic positions, and 57 have obtained NIH research grant support.

Emphasis on three areas of the Clinical Research Program will continue in 1987: electronic communications among Centers, the use of outpatient research protocols, and the clinical research data management and analysis system (CLINFO).

The Biomedical Research Technology (BRT) Program supports research centers, resource-related research projects, and research contracts in three program areas: computer resources, biomedical engineering, and biological structure and function. Examples of research accomplishments follow.

Computers simulate toxic and carcinogenic effects of chemicals in an effort to set realistic safety standards for the environment and for human consumption. Investigators supported through the BRT Program are seeking methods for comparing chemical and physical properties of new compounds with those of known toxic substances.

Three-dimensional information about the structure of cells, cell clusters, nerve nets, and tumors is vitally important in the understanding of hormone production, the progress of cancer, or the causes of many diseases of the nervous system, among others. Now, BRT researchers have developed ways to obtain this information through use of very advanced computer hardware and automated pattern recognition techniques in experiments in brain and tumor anatomy.

In a major advance, rhinoviruses, responsible for the common cold, turn out to have very similar structures to both human poliovirus and some plant viruses. It may be that the similarities indicate similar modes of action. The researchers involved in this discovery used the DRR-sponsored synchrotron radiation resource and a supercomputer.

DRR's Laboratory Animal Science and Primate Research Program comprises three components: the Regional Primate Research Centers, the Laboratory Animal Sciences Program, and the Biological Models and Materials Resources Program. The report requested by the Committee on the needs of the Primate Research Centers details the timetables for renovations and improvements required for continued effective operation of these major research resources.

Research continues in several Primate Research Centers on simian acquired immunodeficiency syndrome (SAIDS). Rhesus monkeys may well provide an excellent model for development and testing of vaccines against retroviruses. The California Center has already succeeded in developing a vaccine that apparently fully protects monkeys against SAIDS. Development of this vaccine will not only benefit the health of the animals but will also further our understanding of how to develop protection against human AIDS. Examples of other research accomplishments in the Centers are: effects of alcohol consumption during pregnancy, and prevention of spread of monkey pox in a colony of rhesus monkeys following the use of a fluorinated pyrimidine compound.

The Laboratory Animal Sciences (LAS) Program assists institutions to develop and improve-animal resources for biomedical research. For example, LAS awards support research on animal diseases, because healthier animals are better research subjects. Maintenance of special colonies and development of animal models assure that important animal resources are available. Resource laboratories are supported in order to improve animal health programs at research institutions. Grants are awarded for training in laboratory animal medicine to assure that key personnel will be available for critical research.

In 1985, DRR initiated a major change in the Animal Facilities Improvement Grants program to assist institutions in complying with requirements for both the Animal Welfare Act and new Department policy on the care and treatment of laboratory animals. For the first time, renovations within facilities improvement awards could be funded in amounts up to $500,000; matching funds were required under the program's guidelines. Twenty-three institutions received improvement awards in 1985; in both 1986 and 1987 approximately nine additional awards will be made.

The newly developed Biological Models and Materials Resources (BMMR) Program supports the research resources which rely on cell systems, lower organisms, and nonbiological models. Support for five such resources initiated in 1985 will continue in both 1986 and 1987.

Since 1972, the Minority Biomedical Research Support (MBRS) Program has addressed the needs of minority research institutions, faculty, and students. In 1985, two new MBRS grant initiatives were instituted; the Thematic Grant provides support for the work of a group of investigators developing research organized around a theme; the Undergraduate College Research Participation Award supports a variety of "enrichment" activities (including visits to the institutions by outside scientists and attendance by students and faculty at scientific meetings and seminars) and individual pilot research projects for faculty. Both new initiatives, as well as the traditional multi-project, multidisciplinary MBRS awards, are continued in 1986 and 1987. Newly available data indicate that 199 former MBRS students have received Ph.D. degrees, 94 have received D.D.S. degrees, and 617 have received M.D. degrees.

The three subcomponents of the Biomedical Research Support (BRS) Program are the Shared Instrumentation Grant, the Minority High School Summer Research Apprentice Program, and the Biomedical Research Support Grant. One hundred seventy-one BRS-Shared Instrumentation Grants were made in 1985; another 156 will be awarded in 1986. These grants support the purchase and installation of sophisticated research equipment that can be shared by groups of PHS-funded investigators. This program is directed at alleviating instrument obsolescence or shortages in the nation's biomedical research laboratories. Equipment purchase between $100,000 and $300,000 is supported. Since 1982 more than 550 research instruments will have been supported. Approximately 200 applications are pending review for funding in 1987; of these we anticipate funding approximately the same number of awards as in 1986.

The Minority High School Summer Research Apprentice Program provides $1,500,000 to approximately 270 research institutions annually to support summer research experiences for 1,000 high school students. The students work for eight weeks in laboratories under the supervision of biomedical researchers; the hope is that apprentices will become aware of the possibility of health research as a career option.

The Biomedical Research Support Grant (BRSG) Program provides flexible funds whose use is determined by the institution. Giving research institutions the opportunity to allocate funds locally enables them to respond quickly to unexpected needs or a sudden change in research emphasis, and to provide seed money in pilot projects for exploration of new theories or techniques. In view of the growing concern for budget control, the Biomedical Research Support Grant Program, is being proposed for elimination in 1987. This program which provides generalized institutional support is of lower priority in comparison to other NIH programs which focus research funds in specific problem areas. In order to assure continued support to research investigators at those institutions most heavily engaged in biomedical research, grantee institutions will be encouraged to require more sharing of resources and facilities, allow more release time for investigators to conduct pilot research activities, initiate institutional development programs for new investigators, and seek additional funds from within the institution and other private sources.

Mr. Chairman, the request for the Division of Research Resources for FY 1987 is $234,192,000. I'll be pleased to answer your questions.

CURRICULUM VITAE

Name: Betty H. Pickett, Ph.D.

Date and Place of Birth: February 15, 1926, Providence, Rhode Island

Marital Status: Married to James McPherson Pickett, 1952

Education: 1945 - A.B. (Psychology) Magna Cum Laude, Brown University
1947 - Sc.M.(Psychology) Brown University
1949 - Ph.D.(Psychology) Brown University

Positions Held:

September 1949 - March 1958	Assistant Professor at University of Minnesota and University of Nebraska; Lecturer in Psychology, University of Connecticut; Professional Associate, Bio-Sciences Information Exchange, Smithsonian Institution, Washington, D.C.
March 1958 March 1961	- Executive Secretary, Behavioral Sciences Study Section; Executive Secretary, Experimental Psychology Study Section, Division of Research Grants, NIH.
August 1962 June 1977	- National Institute of Mental Health: Research Consultant to Mental Health Unit, Region #1; Executive Secretary, Research Career Program; Chief, Cognition and Learning Section, Behavioral Sciences Research Branch; Deputy Director, Division of Extramural Research Programs; Director, Division of Special Mental Health Programs; Acting Director, Division of Extramural Research Programs.
June 1977 January 1979	- Associate Director for Extramural and Collaborative Research Program, National Institute on Aging
January 1979 July 1981	- Deputy Director, National Institute of Child Health and Human Development
July 1981 July 1982	- Acting Director, National Institute of Child Health and Human Development
July 1982 September 1982	- Deputy Director, National Institute of Child Health and Human Development
October 1982 Present	- Director, Division of Research Resources

Professional Societies: American Psychological Association; Eastern Psychological Association; Psychonomic Society; Association of Women in Science; American Association for the Advancement of Science; Academy of Behavioral Medicine.

Honors, Awards: Phi Beta Kappa, 1945. Sigma Xi, 1945. University Fellowship, Brown University, 1947-48. A.B., Brown University, Magna Cum Laude, high honors in psychology. DHEW Superior Service Award, 1972. DHEW Distinguished Service Award, 1975. FEW Award for Distinguished Service in Support of Equal Opportunities for Women, 1975. Citation from Graduate School, Brown University for scientific and professional achievement, 1978. Harold M. Hildreth Award, 1979, American Psychological Association (for distinguished contribution to psychology in the public service). Senior Executive Bonus Award for outstanding performance, 1981, 1982, 1983 and 1984.

DRR MECHANISM TABLE

Mr. NATCHER. Thank you very much.

Now, if you will, please, insert at this point in the record a more detailed breakdown of the table on pages 272 and 173 of your justification, and if you will, include the figures for 1985.

[The information follows:]

Research Resources

Budget Mechanism
(Dollars in Thousands)

	1985 Actual 1/		1986 Appropriation 2/3/		1986 Available after Sequestering 2/4/		1986 Revised 2/4/		1987	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research grants:										
Research Centers										
Clinical research.............	78	$ 86,805	78	$ 89,896	78	$ 86,031	78	$ 86,031	76	$ 86,082
Biomedical research technology	61	34,962	61	35,632	61	34,100	61	34,100	60	33,898
Laboratory animal sciences and primate research............	46	28,869	46	30,346	46	29,041	46	29,041	46	29,905
Subtotal, research centers..........	185	150,636	185	155,874	185	149,172	185	149,172	182	149,885
Other research										
Research Career Programs......	6	324	6	346	6	331	6	331	6	346
Biomedical research support...	728	95,733	720	95,500	713	91,393	713	91,393	154	32,883
(BRS formula)...............	(557)	(62,653)	(557)	(62,260)	(557)	(59,519)	(551)	(59,519)	(---)	(---)
(SIG).......................	(171)	(31,568)	(163)	(31,740)	(156)	(30,374)	(156)	(30,374)	(154)	(31,383)
(MHSSA).....................	(---)	(1,512)	(---)	(1,500)	(---)	(1,500)	(---)	(1,500)	(---)	(1,500)
Minority biomedical research support....................	95	24,576	92	24,951	92	23,878	92	23,878	92	24,149
Other research related........	89	16,901	76	12,487	76	11,950	76	11,950	76	12,122
Subtotal, other research..	918	137,534	894	133,284	887	127,552	887	127,552	328	69,500
Total, research grants.	1,103	288,170	1,079	289,158	1,072	276,724	1,072	276,724	510	219,385

Budget Mechanism (continued)

Training										
Individual awards										
Noncompeting..................	1	12	3	84	3	81	3	81	3	84
Competing:										
New..........................	3	79	--		--		--		--	
Subtotal, individual......	4	91	3	84	3	81	3	81	3	84
Institutional awards:										
Noncompeting..................	23	638	36	991	34	948	34	948	16	453
Competing:										
Renewal.....................	12	346	--	---	--	---	--	---	19	538
New..........................	--	---	--	---	--	---	--	---	--	---
Subtotal, institutional ..	35	984	36	991	34	948	34	948	35	991
Total Training..................	39	1,075	39	1,075	37	1,029	37	1,029	38	1,075
Research and development contracts	4	5,103	6	5,189	6	4,965	6	4,965	6	5,031
Research management and support.........................	FTEs 91	8,291		8,514		8,034	FTEs 91	8,034	FTEs 91	8,701
TOTAL.........................		302,639		303,936		290,752		290,752		234,192

1/ Reflects a comparable transfer of $2,802,000 to the Office of the Assistant Secretary for Health for AIDS research.

2/ Reflects an enacted administrative reduction of $29,000.

3/ Reflects a comparable transfer of $1,731,000 to the Office of the Assistant Secretary for Health for AIDS research.

4/ Reflects a comparable transfer of $1,657,000 to the Office of the Assistant Secretary for Health for AIDS research and a consultant services (Section 515 of the Treasury-Postal Service Appropriation Act, 1985) withholding of $114,000.

BIOMEDICAL RESEARCH SUPPORT GRANTS

Mr. NATCHER. The 1987 budget proposes to terminate the biomedical research support grant for which $62,260,000 was appropriated for 1986 and $59,519,000 is available after sequestration.

If you will update the list of awards on page 577, 596 of last year's hearings, and include the dollar amount of the grant to each institution.

[The information follows:]

1986 BIOMEDICAL RESEARCH SUPPORT GRANT AWARDS

GRANT NO.	INSTITUTION	
AMT AWARDED	CITY	STATE
S07RR05300	UNIVERSITY OF ALABAMA AT BIRMINGHAM	
174,862	BIRMINGHAM	ALABAMA
S07RR05303	UNIVERSITY OF SOUTHERN CALIFORNIA	
61,509	LOS ANGELES	CALIFORNIA
S07RR05304	UNIVERSITY OF CALIFORNIA LOS ANGELES	
65,265	LOS ANGELES	CALIFORNIA
S07RR05305	UNIVERSITY OF CALIFORNIA SAN FRANCISCO	
59,637	SAN FRANCISCO	CALIFORNIA
S07RR05306	GEORGETOWN UNIVERSITY	
15,818	WASHINGTON	DIST OF COL
S07RR05308	EMORY UNIVERSITY	
50,458	ATLANTA	GEORGIA
S07RR05311	NORTHWESTERN UNIVERSITY	
61,982	CHICAGO	ILLINOIS
S07RR05313	UNIVERSITY OF IOWA	
104,143	IOWA CITY	IOWA
S07RR05317	UNIVERSITY OF MARYLAND AT BALTIMORE	
25,891	BALTIMORE	MARYLAND
S07RR05318	HARVARD UNIVERSITY	
38,934	BOSTON	MASSACHUSETTS
S07RR05321	UNIVERSITY OF MICHIGAN AT ANN ARBOR	
82,685	ANN ARBOR	MICHIGAN
S07RR05322	UNIVERSITY OF MINNESOTA OF MNPLS-ST PAUL	
49,706	MINNEAPOLIS	MINNESOTA
S07RR05330	STATE UNIVERSITY OF NEW YORK AT BUFFALO	
78,101	BUFFALO	NEW YORK
S07RR05331	COLUMBIA UNIVERSITY NEW YORK	
97,108	NEW YORK	NEW YORK
S07RR05332	NEW YORK UNIVERSITY	
26,451	NEW YORK	NEW YORK
S07RR05333	UNIVERSITY OF NORTH CAROLINA CHAPEL HILL	
89,102	CHAPEL HILL	NORTH CAROLINA
S07RR05335	CASE WESTERN RESERVE UNIVERSITY	
14,682	CLEVELAND	OHIO
S07RR05336	OREGON HEALTH SCIENCES UNIVERSITY	
14,278	PORTLAND	OREGON
S07RR05337	UNIVERSITY OF PENNSYLVANIA	
136,775	PHILADELPHIA	PENNSYLVANIA
S07RR05338	UNIVERSITY OF PITTSBURGH	
22,202	PITTSBURGH	PENNSYLVANIA
S07RR05339	TEMPLE UNIVERSITY	
12,912	PHILADELPHIA	PENNSYLVANIA
S07RR05346	UNIVERSITY OF WASHINGTON	
107,027	SEATTLE	WASHINGTON
S07RR05349	UNIVERSITY OF ALABAMA AT BIRMINGHAM	
291,522	BIRMINGHAM	ALABAMA
S07RR05350	UNIVERSITY OF ARKANSAS MED SCIS LTL ROCK	
80,557	LITTLE ROCK	ARKANSAS
S07RR05351	UNIVERSITY OF CALIFORNIA IRVINE	
232,918	IRVINE	CALIFORNIA
S07RR05352	LOMA LINDA UNIVERSITY	
48,102	LOMA LINDA	CALIFORNIA
S07RR05353	STANFORD UNIVERSITY	
348,980	STANFORD	CALIFORNIA

S07RR05354	UNIVERSITY OF CALIFORNIA LOS ANGELES	315,112	LOS ANGELES	CALIFORNIA
S07RR05355	UNIVERSITY OF CALIFORNIA SAN FRANCISCO	350,368	SAN FRANCISCO	CALIFORNIA
S07RR05356	UNIVERSITY OF SOUTHERN CALIFORNIA	291,401	LOS ANGELES	CALIFORNIA
S07RR05357	UNIVERSITY OF COLORADO HLTH SCIENCES CTR	292,286	DENVER	COLORADO
S07RR05358	YALE UNIVERSITY	341,395	NEW HAVEN	CONNECTICUT
S07RR05359	GEORGE WASHINGTON UNIVERSITY	155,429	WASHINGTON	DIST OF COL
S07RR05360	GEORGETOWN UNIVERSITY	184,843	WASHINGTON	DIST OF COL
S07RR05361	HOWARD UNIVERSITY	60,415	WASHINGTON	DIST OF COL
S07RR05362	UNIVERSITY OF FLORIDA	246,782	GAINESVILLE	FLORIDA
S07RR05363	UNIVERSITY OF MIAMI	288,152	MIAMI	FLORIDA
S07RR05364	EMORY UNIVERSITY	272,908	ATLANTA	GEORGIA
S07RR05365	MEDICAL COLLEGE OF GEORGIA	144,094	AUGUSTA	GEORGIA
S07RR05366	UNIVERSITY OF HLTH SCI/CHICAGO MED SCH	99,749	NORTH CHICAGO	ILLINOIS
S07RR05367	UNIVERSITY OF CHICAGO	312,577	CHICAGO	ILLINOIS
S07RR05368	LOYOLA UNIVERSITY MEDICAL CENTER	78,342	MAYWOOD	ILLINOIS
S07RR05369	UNIVERSITY OF ILLINOIS AT CHICAGO	248,631	CHICAGO	ILLINOIS
S07RR05370	NORTHWESTERN UNIVERSITY	255,528	CHICAGO	ILLINOIS
S07RR05371	INDIANA UNIV-PURDUE UNIV AT INDIANAPOLIS	238,751	INDIANAPOLIS	INDIANA
S07RR05372	UNIVERSITY OF IOWA	295,860	IOWA CITY	IOWA
S07RR05373	UNIVERSITY OF KANSAS COL HLTH SCI & HOSP	153,324	KANSAS CITY	KANSAS
S07RR05374	UNIVERSITY OF KENTUCKY	159,910	LEXINGTON	KENTUCKY
S07RR05375	UNIVERSITY OF LOUISVILLE	55,125	LOUISVILLE	KENTUCKY
S07RR05376	LOUISIANA STATE UNIV MED CTR NEW ORLEANS	195,907	NEW ORLEANS	LOUISIANA
S07RR05377	TULANE UNIVERSITY OF LOUISIANA	121,425	NEW ORLEANS	LOUISIANA
S07RR05378	JOHNS HOPKINS UNIVERSITY	360,109	BALTIMORE	MARYLAND
S07RR05379	UNIVERSITY OF MARYLAND AT BALTIMORE	283,083	BALTIMORE	MARYLAND
S07RR05380	BOSTON UNIVERSITY	294,143	BOSTON	MASSACHUSETTS
S07RR05381	HARVARD UNIVERSITY	316,322	BOSTON	MASSACHUSETTS
S07RR05382	TUFTS UNIVERSITY	287,387	BOSTON	MASSACHUSETTS

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S07RR05383 UNIVERSITY OF MICHIGAN AT ANN ARBOR
  315,604    ANN ARBOR           MICHIGAN
S07RR05384 WAYNE STATE UNIVERSITY
  202,737    DETROIT             MICHIGAN
S07RR05385 UNIVERSITY OF MINNESOTA OF MNPLS-ST PAUL
  307,295    MINNEAPOLIS         MINNESOTA
S07RR05386 UNIVERSITY OF MISSISSIPPI MEDICAL CENTER
  105,098    JACKSON             MISSISSIPPI
S07RR05387 UNIVERSITY OF MISSOURI COLUMBIA
  147,633    COLUMBIA            MISSOURI
S07RR05388 ST. LOUIS UNIVERSITY
  166,964    SAINT LOUIS         MISSOURI
S07RR05389 WASHINGTON UNIVERSITY
  330,509    SAINT LOUIS         MISSOURI
S07RR05390 CREIGHTON UNIVERSITY
   35,733    OMAHA               NEBRASKA
S07RR05391 UNIVERSITY OF NEBRASKA MEDICAL CENTER
   89,280    OMAHA               NEBRASKA
S07RR05392 DARTMOUTH COLLEGE
  226,172    HANOVER             NEW HAMPSHIRE
S07RR05393 UNIVERSITY OF MEDICINE & DENTISTRY OF NJ
  171,360    NEWARK              NEW JERSEY
S07RR05394 ALBANY MEDICAL COLLEGE OF UNION UNIV
  161,613    ALBANY              NEW YORK
S07RR05395 COLUMBIA UNIVERSITY NEW YORK
  324,704    NEW YORK            NEW YORK
S07RR05396 CORNELL UNIVERSITY MEDICAL CENTER
  295,394    NEW YORK            NEW YORK
S07RR05397 YESHIVA UNIVERSITY
  330,616    NEW YORK            NEW YORK
S07RR05398 NEW YORK MEDICAL COLLEGE
  181,172    VALHALLA            NEW YORK
S07RR05399 NEW YORK UNIVERSITY
  314,693    NEW YORK            NEW YORK
S07RR05400 STATE UNIVERSITY OF NEW YORK AT BUFFALO
  204,836    BUFFALO             NEW YORK
S07RR05401 DOWNSTATE MEDICAL CENTER
  160,815    NEW YORK            NEW YORK
S07RR05402 UPSTATE MEDICAL CENTER
  140,699    SYRACUSE            NEW YORK
S07RR05403 UNIVERSITY OF ROCHESTER
  305,628    ROCHESTER           NEW YORK
S07RR05404 WAKE FOREST UNIVERSITY
  230,137    WINSTON-SALEM       NORTH CAROLINA
S07RR05405 DUKE UNIVERSITY
  326,821    DURHAM              NORTH CAROLINA
S07RR05406 UNIVERSITY OF NORTH CAROLINA CHAPEL HILL
  301,934    CHAPEL HILL         NORTH CAROLINA
S07RR05407 UNIVERSITY OF NORTH DAKOTA
   20,742    GRAND FORKS         NORTH DAKOTA
S07RR05408 UNIVERSITY OF CINCINNATI
  283,958    CINCINNATI          OHIO
S07RR05409 OHIO STATE UNIVERSITY
  161,198    COLUMBUS            OHIO
S07RR05410 CASE WESTERN RESERVE UNIVERSITY
  301,366    CLEVELAND           OHIO
S07RR05411 UNIVERSITY OF OKLAHOMA HLTH SCIENCES CTR
  122,676    OKLAHOMA CITY       OKLAHOMA
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S07RR05412	OREGON HEALTH SCIENCES UNIVERSITY	
210,854	PORTLAND	OREGON
S07RR05413	HAHNEMANN UNIVERSITY	
171,262	PHILADELPHIA	PENNSYLVANIA
S07RR05414	THOMAS JEFFERSON UNIVERSITY	
149,268	PHILADELPHIA	PENNSYLVANIA
S07RR05415	UNIVERSITY OF PENNSYLVANIA	
331,156	PHILADELPHIA	PENNSYLVANIA
S07RR05416	UNIVERSITY OF PITTSBURGH	
300,912	PITTSBURGH	PENNSYLVANIA
S07RR05417	TEMPLE UNIVERSITY	
226,279	PHILADELPHIA	PENNSYLVANIA
S07RR05418	MEDICAL COLLEGE OF PENNSYLVANIA	
139,669	PHILADELPHIA	PENNSYLVANIA
S07RR05419	UNIVERSITY OF PUERTO RICO MED SCIENCES	
73,223	SAN JUAN	PUERTO RICO
S07RR05420	MEDICAL UNIVERSITY OF SOUTH CAROLINA	
156,856	CHARLESTON	SOUTH CAROLINA
S07RR05421	UNIVERSITY OF SOUTH DAKOTA	
14,449	VERMILLION	SOUTH DAKOTA
S07RR05422	MEHARRY MEDICAL COLLEGE	
46,478	NASHVILLE	TENNESSEE
S07RR05423	UNIVERSITY OF TENN CENTER HEALTH SCIEN	
203,098	MEMPHIS	TENNESSEE
S07RR05424	VANDERBILT UNIVERSITY	
290,926	NASHVILLE	TENNESSEE
S07RR05425	BAYLOR COLLEGE OF MEDICINE	
308,252	HOUSTON	TEXAS
S07RR05426	UNIVERSITY OF TEXAS HLTH SCI CTR DALLAS	
286,119	DALLAS	TEXAS
S07RR05427	UNIVERSITY OF TEXAS MED BR GALVESTON	
203,937	GALVESTON	TEXAS
S07RR05428	UNIVERSITY OF UTAH	
287,322	SALT LAKE CITY	UTAH
S07RR05429	UNIVERSITY OF VERMONT & ST AGRIC COLLEGE	
235,714	BURLINGTON	VERMONT
S07RR05430	VIRGINIA COMMONWEALTH UNIVERSITY	
283,862	RICHMOND	VIRGINIA
S07RR05431	UNIVERSITY OF VIRGINIA CHARLOTTESVILLE	
284,578	CHARLOTTESVILLE	VIRGINIA
S07RR05432	UNIVERSITY OF WASHINGTON	
326,707	SEATTLE	WASHINGTON
S07RR05433	WEST VIRGINIA UNIVERSITY	
99,870	MORGANTOWN	WEST VIRGINIA
S07RR05434	MEDICAL COLLEGE OF WISCONSIN	
223,292	MILWAUKEE	WISCONSIN
S07RR05435	UNIVERSITY OF WISCONSIN MADISON	
296,886	MADISON	WISCONSIN
S07RR05441	UNIVERSITY OF CALIFORNIA BERKELEY	
82,845	BERKELEY	CALIFORNIA
S07RR05442	UNIVERSITY OF CALIFORNIA LOS ANGELES	
15,913	LOS ANGELES	CALIFORNIA
S07RR05443	YALE UNIVERSITY	
111,727	NEW HAVEN	CONNECTICUT
S07RR05444	TULANE UNIVERSITY OF LOUISIANA	
30,688	NEW ORLEANS	LOUISIANA
S07RR05445	JOHNS HOPKINS UNIVERSITY	
261,622	BALTIMORE	MARYLAND

S07RR05446	HARVARD UNIVERSITY	241,149	BOSTON	MASSACHUSETTS
S07RR05447	UNIVERSITY OF MICHIGAN AT ANN ARBOR	43,158	ANN ARBOR	MICHIGAN
S07RR05448	UNIVERSITY OF MINNESOTA OF MNPLS-ST PAUL	143,130	MINNEAPOLIS	MINNESOTA
S07RR05449	COLUMBIA UNIVERSITY NEW YORK	135,639	NEW YORK	NEW YORK
S07RR05450	UNIVERSITY OF NORTH CAROLINA CHAPEL HILL	47,677	CHAPEL HILL	NORTH CAROLINA
S07RR05451	UNIVERSITY OF PITTSBURGH	111,082	PITTSBURGH	PENNSYLVANIA
S07RR05453	UNIVERSITY OF CALIFORNIA SAN FRANCISCO	166,646	SAN FRANCISCO	CALIFORNIA
S07RR05454	STATE UNIVERSITY OF NEW YORK AT BUFFALO	46,656	BUFFALO	NEW YORK
S07RR05456	UNIVERSITY OF WISCONSIN MADISON	59,825	MADISON	WISCONSIN
S07RR05457	UNIVERSITY OF CALIFORNIA DAVIS	66,803	DAVIS	CALIFORNIA
S07RR05458	COLORADO STATE UNIVERSITY	85,177	FORT COLLINS	COLORADO
S07RR05460	UNIVERSITY OF ILLINOIS URBANA-CHAMPAIGN	52,726	CHAMPAIGN	ILLINOIS
S07RR05462	CORNELL UNIVERSITY ITHACA	124,252	ITHACA	NEW YORK
S07RR05463	OHIO STATE UNIVERSITY	52,140	COLUMBUS	OHIO
S07RR05464	UNIVERSITY OF PENNSYLVANIA	124,654	PHILADELPHIA	PENNSYLVANIA
S07RR05465	WASHINGTON STATE UNIVERSITY	39,726	PULLMAN	WASHINGTON
S07RR05466	LOS ANGELES COUNTY-UNIV OF S CAL MED CTR	24,863	LOS ANGELES	CALIFORNIA
S07RR05467	CHILDREN'S HOSPITAL MED CTR NORTHERN CA	55,198	OAKLAND	CALIFORNIA
S07RR05468	CEDARS-SINAI MEDICAL CENTER	67,533	LOS ANGELES	CALIFORNIA
S07RR05469	CHILDREN'S HOSPITAL OF LOS ANGELES	74,065	LOS ANGELES	CALIFORNIA
S07RR05471	CITY OF HOPE NATIONAL MEDICAL CENTER	82,527	DUARTE	CALIFORNIA
S07RR05472	MOUNT ZION HOSPITAL AND MEDICAL CENTER	16,262	SAN FRANCISCO	CALIFORNIA
S07RR05476	MICHAEL REESE HOSP & MED CTR (CHICAGO)	100,979	CHICAGO	ILLINOIS
S07RR05477	RUSH UNIVERSITY	171,344	CHICAGO	ILLINOIS
S07RR05479	BETH ISRAEL HOSP (BOSTON)	202,015	BOSTON	MASSACHUSETTS
S07RR05483	FORSYTH DENTAL CENTER	118,091	BOSTON	MASSACHUSETTS
S07RR05484	MC LEAN HOSPITAL (BELMONT, MA)	152,799	BELMONT	MASSACHUSETTS
S07RR05485	MASSACHUSETTS EYE AND EAR INFIRMARY	129,630	BOSTON	MASSACHUSETTS
S07RR05486	MASSACHUSETTS GENERAL HOSPITAL	299,792	BOSTON	MASSACHUSETTS

S07RR05487	UNIVERSITY HOSPITAL (BOSTON)	91,332	BOSTON	MASSACHUSETTS
S07RR05490	HENRY FORD HOSPITAL	67,314	DETROIT	MICHIGAN
S07RR05491	JEWISH HOSPITAL OF ST. LOUIS	113,801	SAINT LOUIS	MISSOURI
S07RR05493	CHILDREN'S HOSPITAL (BUFFALO)	18,631	BUFFALO	NEW YORK
S07RR05495	HOSPITAL FOR SPECIAL SURGERY	51,965	NEW YORK	NEW YORK
S07RR05496	LONG ISLAND JEWISH-HILLSIDE MEDICAL CTR	62,428	NEW HYDE PARK	NEW YORK
S07RR05498	MARY IMOGENE BASSETT HOSPITAL	20,125	COOPERSTOWN	NEW YORK
S07RR05499	MONTEFIORE MEDICAL CENTER (BRONX, NY)	124,149	NEW YORK	NEW YORK
S07RR05506	CHILDREN'S HOSPITAL OF PHILADELPHIA	164,747	PHILADELPHIA	PENNSYLVANIA
S07RR05507	CHILDREN'S HOSPITAL OF PITTSBURGH	49,055	PITTSBURGH	PENNSYLVANIA
S07RR05510	WILLS EYE HOSPITAL (PHILADELPHIA)	22,318	PHILADELPHIA	PENNSYLVANIA
S07RR05511	UNIVERSITY OF TEXAS SYSTEM CANCER CENTER	284,366	HOUSTON	TEXAS
S07RR05513	PALO ALTO MEDICAL FOUNDATION RES INST	31,588	PALO ALTO	CALIFORNIA
S07RR05514	SCRIPPS CLINIC AND RESEARCH FOUNDATION	302,139	LA JOLLA	CALIFORNIA
S07RR05515	CHILDREN'S HOSP NATL MED CTR (WASH, DC)	40,019	WASHINGTON	DIST OF COL
S07RR05517	MENNINGER FOUNDATION	22,609	TOPEKA	KANSAS
S07RR05518	ALTON OCHSNER MEDICAL FOUNDATION	23,155	NEW ORLEANS	LOUISIANA
S07RR05519	SOUTHWEST FOUNDATION FOR BIOMEDICAL RES	89,486	SAN ANTONIO	TEXAS
S07RR05520	PACIFIC NORTHWEST RESEARCH FOUNDATION	23,853	SEATTLE	WASHINGTON
S07RR05521	KAISER FOUNDATION RESEARCH INSTITUTE	54,813	OAKLAND	CALIFORNIA
S07RR05522	SRI INTERNATIONAL	148,626	MENLO PARK	CALIFORNIA
S07RR05526	DANA-FARBER CANCER INSTITUTE	289,841	BOSTON	MASSACHUSETTS
S07RR05527	EYE RESEARCH INSTITUTE OF RETINA FDN	147,402	BOSTON	MASSACHUSETTS
S07RR05528	WORCESTER FOUNDATION FOR EXPER BIOLOGY	185,357	SHREWSBURY	MASSACHUSETTS
S07RR05529	MICHIGAN CANCER FOUNDATION	112,170	DETROIT	MICHIGAN
S07RR05530	MAYO FOUNDATION	295,767	ROCHESTER	MINNESOTA
S07RR05533	PUBLIC HLTH RES INST OF THE CITY OF NY	93,404	NEW YORK	NEW YORK
S07RR05534	SLOAN-KETTERING INSTITUTE FOR CANCER RES	292,583	NEW YORK	NEW YORK
S07RR05535	CHILDREN'S HOSPITAL MED CTR (CINCINNATI)	93,015	CINCINNATI	OHIO

S07RR05538	OKLAHOMA MEDICAL RESEARCH FOUNDATION	
133,413	OKLAHOMA CITY	OKLAHOMA
S07RR05539	INSTITUTE FOR CANCER RESEARCH	
141,838	PHILADELPHIA	PENNSYLVANIA
S07RR05540	WISTAR INSTITUTE OF ANATOMY AND BIOLOGY	
253,108	PHILADELPHIA	PENNSYLVANIA
S07RR05541	UNIVERSITY OF TENNESSEE KNOXVILLE	
18,278	KNOXVILLE	TENNESSEE
S07RR05545	JACKSON LABORATORY	
166,046	BAR HARBOR	MAINE
S07RR05546	FRIENDS MEDICAL SCIENCE RESEARCH CENTER	
29,423	CATONSVILLE	MARYLAND
S07RR05547	MARINE BIOLOGICAL LABORATORY	
56,784	WOODS HOLE	MASSACHUSETTS
S07RR05548	EASTMAN DENTAL CENTER	
11,762	ROCHESTER	NEW YORK
S07RR05551	LOS ANGELES COUNTY HARBOR-UCLA MED CTR	
169,330	TORRANCE	CALIFORNIA
S07RR05564	UNIVERSITY OF ILLINOIS AT CHICAGO	
27,221	CHICAGO	ILLINOIS
S07RR05566	MEDICAL RESEARCH INSTITUTE OF SAN FRAN	
87,204	SAN FRANCISCO	CALIFORNIA
S07RR05569	BOSTON CITY HOSPITAL	
52,217	BOSTON	MASSACHUSETTS
S07RR05570	MAGEE-WOMEN'S HOSPITAL	
19,075	PITTSBURGH	PENNSYLVANIA
S07RR05571	UNIVERSITY OF MICHIGAN AT ANN ARBOR	
19,238	ANN ARBOR	MICHIGAN
S07RR05573	UNIVERSITY OF FLORIDA	
49,931	GAINESVILLE	FLORIDA
S07RR05576	UNIV OF MED/DENT NJ-RUTGERS MEDICAL SCH	
174,012	PISCATAWAY	NEW JERSEY
S07RR05583	UNIVERSITY OF NEW MEXICO ALBUQUERQUE	
168,084	ALBUQUERQUE	NEW MEXICO
S07RR05584	ST. JUDE CHILDREN'S RESEARCH HOSPITAL	
161,865	MEMPHIS	TENNESSEE
S07RR05586	PURDUE UNIVERSITY WEST LAFAYETTE	
81,827	WEST LAFAYETTE	INDIANA
S07RR05587	ST. ELIZABETH'S HOSPITAL OF BOSTON	
42,476	BOSTON	MASSACHUSETTS
S07RR05588	VIRGINIA MASON RESEARCH CENTER	
23,115	SEATTLE	WASHINGTON
S07RR05589	HOSPITAL FOR JOINT DISEASES ORTHO INST	
41,389	NEW YORK	NEW YORK
S07RR05590	PENNSYLVANIA HOSPITAL (PHILADELPHIA)	
34,218	PHILADELPHIA	PENNSYLVANIA
S07RR05591	NEW ENGLAND DEACONESS HOSPITAL	
88,087	BOSTON	MASSACHUSETTS
S07RR05592	MONTEFIORE HOSPITAL (PITTSBURGH)	
42,987	PITTSBURGH	PENNSYLVANIA
S07RR05593	GOOD SAMARITAN HOSP & MED CTR(PRTLND,OR)	
56,715	PORTLAND	OREGON
S07RR05594	UNIVERSITY OF MISSISSIPPI	
32,412	UNIVERSITY	MISSISSIPPI
S07RR05595	SALK INSTITUTE FOR BIOLOGICAL STUDIES	
257,843	LA JOLLA	CALIFORNIA
S07RR05596	HASKINS LABORATORIES	
51,709	NEW HAVEN	CONNECTICUT

S07RR05598	NEW ENGLAND MEDICAL CENTER HOSPITALS,INC	181,167	BOSTON	MASSACHUSETTS
S07RR05599	UNIVERSITY OF HAWAII AT MANOA	34,164	HONOLULU	HAWAII
S07RR05604	UNIVERSITY OF CALIFORNIA SAN FRANCISCO	29,284	SAN FRANCISCO	CALIFORNIA
S07RR05605	UNIVERSITY OF ARIZONA	48,928	TUCSON	ARIZONA
S07RR05606	UNIVERSITY OF KANSAS LAWRENCE	53,354	LAWRENCE	KANSAS
S07RR05607	OHIO STATE UNIVERSITY	36,360	COLUMBUS	OHIO
S07RR05610	PRESBYTERIAN-UNIVERSITY OF PA MED CTR	50,255	PHILADELPHIA	PENNSYLVANIA
S07RR05611	PHILADELPHIA GERIATRIC CTR-FRIEDMAN HOSP	62,354	PHILADELPHIA	PENNSYLVANIA
S07RR05612	OREGON RESEARCH INSTITUTE	51,495	EUGENE	OREGON
S07RR05623	MICHIGAN STATE UNIVERSITY	62,859	EAST LANSING	MICHIGAN
S07RR05626	CENTER FOR BLOOD RESEARCH	91,625	BOSTON	MASSACHUSETTS
S07RR05629	EVANSTON HOSPITAL	27,228	EVANSTON	ILLINOIS
S07RR05634	UNIVERSITY OF MINNESOTA OF MNPLS-ST PAUL	38,541	MINNEAPOLIS	MINNESOTA
S07RR05635	UNIVERSITY OF WASHINGTON	44,221	SEATTLE	WASHINGTON
S07RR05644	RHODE ISLAND HOSPITAL (PROVIDENCE, RI)	75,943	PROVIDENCE	RHODE ISLAND
S07RR05648	ROSWELL PARK MEMORIAL INSTITUTE	285,613	BUFFALO	NEW YORK
S07RR05649	NEW YORK STATE DEPT OF HEALTH	134,156	ALBANY	NEW YORK
S07RR05650	NEW YORK STATE PSYCHIATRIC INSTITUTE	192,556	NEW YORK	NEW YORK
S07RR05651	NATHAN S. KLINE INSTITUTE FOR PSYCH RES	12,793	ORANGEBURG	NEW YORK
S07RR05653	MOUNT SINAI SCHOOL OF MEDICINE	294,496	NEW YORK	NEW YORK
S07RR05654	UNIVERSITY OF TEXAS HLTH SCI CTR SAN ANT	214,384	SAN ANTONIO	TEXAS
S07RR05655	CHILDREN'S ORTHOPEDIC HOSPITAL-MED CTR	47,182	SEATTLE	WASHINGTON
S07RR05656	MICHIGAN STATE UNIVERSITY	118,053	EAST LANSING	MICHIGAN
S07RR05658	MOUNT SINAI MEDICAL CENTER	23,007	CLEVELAND	OHIO
S07RR05662	MOUNT SINAI MEDICAL CENTER (MIAMI BEACH)	31,583	MIAMI BEACH	FLORIDA
S07RR05664	BROWN UNIVERSITY	131,925	PROVIDENCE	RHODE ISLAND
S07RR05665	UNIVERSITY OF CALIFORNIA SAN DIEGO	316,400	LA JOLLA	CALIFORNIA
S07RR05673	JOSLIN DIABETES CENTER	114,123	BOSTON	MASSACHUSETTS
S07RR05674	CLEVELAND CLINIC FOUNDATION	159,392	CLEVELAND	OHIO

S07RR05675	UNIVERSITY OF ARIZONA	
235,983	TUCSON	ARIZONA
S07RR05676	SOUTHERN RESEARCH INSTITUTE	
93,284	BIRMINGHAM	ALABAMA
S07RR05677	UNIVERSITY OF CONNECTICUT HEALTH CENTER	
124,732	FARMINGTON	CONNECTICUT
S07RR05678	UNIVERSITY OF CONNECTICUT HEALTH CENTER	
271,964	FARMINGTON	CONNECTICUT
S07RR05680	PENNSYLVANIA STATE UNIV HERSHEY MED CTR	
274,443	HERSHEY	PENNSYLVANIA
S07RR05684	UNIVERSITY OF CALIFORNIA DAVIS	
192,568	DAVIS	CALIFORNIA
S07RR05688	NEW YORK BLOOD CENTER	
68,709	NEW YORK	NEW YORK
S07RR05689	AMERICAN DENTAL ASSN HEALTH FDN	
39,393	CHICAGO	ILLINOIS
S07RR05692	JOHN B. PIERCE FOUNDATION LAB, INC.	
48,545	NEW HAVEN	CONNECTICUT
S07RR05694	MEDICAL RESEARCH FOUNDATION OF OREGON	
97,576	PORTLAND	OREGON
S07RR05697	VIRGINIA COMMONWEALTH UNIVERSITY	
68,582	RICHMOND	VIRGINIA
S07RR05700	MEDICAL COLLEGE OF OHIO AT TOLEDO	
100,016	TOLEDO	OHIO
S07RR05704	LOUISIANA STATE UNIV MED CTR NEW ORLEANS	
48,565	NEW ORLEANS	LOUISIANA
S07RR05705	TRUDEAU INSTITUTE, INC.	
40,295	SARANAC LAKE	NEW YORK
S07RR05710	RAND CORPORATION	
38,986	SANTA MONICA	CALIFORNIA
S07RR05711	BOSTON BIOMEDICAL RESEARCH INSTITUTE	
138,364	BOSTON	MASSACHUSETTS
S07RR05712	UNIVERSITY OF MASSACHUSETTS MEDICAL SCH	
287,917	WORCESTER	MASSACHUSETTS
S07RR05714	UNIVERSITY OF WASHINGTON	
91,514	SEATTLE	WASHINGTON
S07RR05716	MEDICAL FOUNDATION OF BUFFALO, INC	
51,472	BUFFALO	NEW YORK
S07RR05717	COLD SPRING HARBOR LABORATORY	
144,681	COLD SPRING HARBO	NEW YORK
S07RR05723	BATTELLE MEMORIAL INSTITUTE	
62,031	COLUMBUS	OHIO
S07RR05724	VIRGINIA COMMONWEALTH UNIVERSITY	
105,635	RICHMOND	VIRGINIA
S07RR05728	UNIVERSITY OF FLORIDA	
63,891	GAINESVILLE	FLORIDA
S07RR05730	EUNICE KENNEDY SHRIVER CTR MTL RETARDATN	
109,315	WALTHAM	MASSACHUSETTS
S07RR05731	ASSOCIATED UNIV-BROOKHAVEN NATL LAB	
118,984	UPTON	NEW YORK
S07RR05736	STATE UNIVERSITY NEW YORK STONY BROOK	
234,399	STONY BROOK	NEW YORK
S07RR05737	AMERICAN NATIONAL RED CROSS	
32,341	WASHINGTON	DIST OF COL
S07RR05738	UNIVERSITY OF UTAH	
65,396	SALT LAKE CITY	UTAH
S07RR05743	UNIVERSITY OF CONNECTICUT STORRS	
40,323	STORRS	CONNECTICUT

S07RR05744	IIT RESEARCH INSTITUTE	37,861	CHICAGO	ILLINOIS
S07RR05745	UNIVERSITY OF TEXAS HLTH SCI CTR HOUSTON	283,691	HOUSTON	TEXAS
S07RR05746	OAK RIDGE ASSOCIATED UNIVERSITIES	19,796	OAK RIDGE	TENNESSEE
S07RR05749	UNIVERSITY OF SOUTH FLORIDA	83,208	TAMPA	FLORIDA
S07RR05753	MEMORIAL HOSPITAL FOR CANCER & ALLIED DI	164,083	NEW YORK	NEW YORK
S07RR05755	UNIVERSITY OF CALIFORNIA SAN FRANCISCO	124,464	SAN FRANCISCO	CALIFORNIA
S07RR05756	UNIVERSITY OF CALIFORNIA LOS ANGELES	206,422	LOS ANGELES	CALIFORNIA
S07RR05758	UNIVERSITY OF WASHINGTON	55,608	SEATTLE	WASHINGTON
S07RR05761	FRED HUTCHINSON CANCER RESEARCH CENTER	220,407	SEATTLE	WASHINGTON
S07RR05765	ROGER WILLIAMS GENERAL HOSPITAL	37,419	PROVIDENCE	RHODE ISLAND
S07RR05767	MEDICAL UNIVERSITY OF SOUTH CAROLINA	67,183	CHARLESTON	SOUTH CAROLINA
S07RR05768	INSTITUTE FOR MED RES SANTA CLARA COUNTY	23,325	SAN JOSE	CALIFORNIA
S07RR05770	UNIVERSITY OF MARYLAND AT BALTIMORE	17,964	BALTIMORE	MARYLAND
S07RR05771	EASTERN VIRGINIA MEDICAL SCHOOL	33,074	NORFOLK	VIRGINIA
S07RR05772	MICHIGAN STATE UNIVERSITY	78,813	EAST LANSING	MICHIGAN
S07RR05773	TEXAS TECH UNIVERSITY	94,695	LUBBOCK	TEXAS
S07RR05774	UNIVERSITY OF SOUTH ALABAMA	126,890	MOBILE	ALABAMA
S07RR05775	AMERICAN HEALTH FOUNDATION	127,410	NEW YORK	NEW YORK
S07RR05776	UNIVERSITY OF ILLINOIS AT CHICAGO	12,942	CHICAGO	ILLINOIS
S07RR05778	STATE UNIVERSITY NEW YORK STONY BROOK	30,604	STONY BROOK	NEW YORK
S07RR05779	EYE AND EAR HOSPITAL OF PITTSBURGH	42,361	PITTSBURGH	PENNSYLVANIA
S07RR05780	CHARLES R. DREW POSTGRADUATE MEDICAL SCH	42,562	LOS ANGELES	CALIFORNIA
S07RR05788	UNIVERSITY OF FLORIDA	64,762	GAINESVILLE	FLORIDA
S07RR05791	RESEARCH TRIANGLE INSTITUTE	43,667	RESEARCH TRIANGLE	NORTH CAROLINA
S07RR05792	UNIVERSITY OF SOUTHERN CALIFORNIA	84,720	LOS ANGELES	CALIFORNIA
S07RR05794	WRIGHT STATE UNIVERSITY	30,721	DAYTON	OHIO
S07RR05795	MEDICAL COLLEGE OF GEORGIA	37,625	AUGUSTA	GEORGIA
S07RR05796	UNIVERSITY OF MICHIGAN AT ANN ARBOR	39,613	ANN ARBOR	MICHIGAN
S07RR05799	CARNEGIE INSTITUTION OF WASHINGTON, DC	58,349	BALTIMORE	MARYLAND

S07RR05801	ALLEGHENY-SINGER RESEARCH INSTITUTE	11,209	PITTSBURGH	PENNSYLVANIA
S07RR05803	LA JOLLA CANCER RESEARCH FOUNDATION	119,676	LA JOLLA	CALIFORNIA
S07RR05804	LDS HOSPITAL	12,383	SALT LAKE CITY	UTAH
S07RR05806	NORTHEASTERN OHIO UNIVERSITIES COLL MED	25,449	ROOTSTOWN	OHIO
S07RR05807	UNIVERSITY OF ALABAMA AT BIRMINGHAM	30,313	BIRMINGHAM	ALABAMA
S07RR05808	KENNEDY INSTITUTE FOR HANDICAPPED CHLDRN	42,185	BALTIMORE	MARYLAND
S07RR05810	ESTELLE DOHENY EYE FOUNDATION	44,902	LOS ANGELES	CALIFORNIA
S07RR05812	EAST CAROLINA UNIVERSITY	49,283	GREENVILLE	NORTH CAROLINA
S07RR05813	UNIVERSITY OF NEVADA RENO	55,084	RENO	NEVADA
S07RR05814	TEXAS AGRI AND MECH UNIV COLLEGE STATION	44,583	COLLEGE STATION	TEXAS
S07RR05815	UNIVERSITY OF SOUTH CAROLINA AT COLUMBIA	21,558	COLUMBIA	SOUTH CAROLINA
S07RR05816	UNIVERSITY OF CALIFORNIA RIVERSIDE	31,356	RIVERSIDE	CALIFORNIA
S07RR05818	MIRIAM HOSPITAL	39,180	PROVIDENCE	RHODE ISLAND
S07RR05821	LOMA LINDA UNIVERSITY	28,306	LOMA LINDA	CALIFORNIA
S07RR05822	LOUISIANA STATE UNIV MED CTR SHREVEPORT	55,222	SHREVEPORT	LOUISIANA
S07RR05823	UNIVERSITY CITY SCIENCE CENTER	85,471	PHILADELPHIA	PENNSYLVANIA
S07RR05825	MONELL CHEMICAL SENSES CENTER	56,258	PHILADELPHIA	PENNSYLVANIA
S07RR05828	UNIVERSITY OF TEXAS HLTH SCI CTR HOUSTON	24,284	HOUSTON	TEXAS
S07RR05829	UNIVERSITY OF ALABAMA AT BIRMINGHAM	13,928	BIRMINGHAM	ALABAMA
S07RR05830	NORTHEASTERN UNIVERSITY	22,199	BOSTON	MASSACHUSETTS
S07RR05831	UNIVERSITY OF COLORADO AT BOULDER	47,140	BOULDER	COLORADO
S07RR05832	UNIVERSITY OF CALIFORNIA BERKELEY	50,834	BERKELEY	CALIFORNIA
S07RR05834	FATHER FLANAGAN'S BOYS' HOME	33,578	BOYS TOWN	NEBRASKA
S07RR05838	INSTITUTE FOR BASIC RES IN DEV DISABIL	64,656	NEW YORK	NEW YORK
S07RR05839	OREGON SOCIAL LEARNING CENTER, INC.	46,007	EUGENE	OREGON
S07RR05840	ST. LUKE'S-ROOSEVELT INST FOR HLTH SCI	66,693	NEW YORK	NEW YORK
S07RR05841	BECKMAN RESEARCH INSTITUTE/CITY OF HOPE	121,637	DUARTE	CALIFORNIA
S07RR05842	NATIONAL JEWISH CTR FOR IMMNLGY/RESP MED	179,931	DENVER	COLORADO
S07RR05843	SOUTHERN ILLINOIS UNIVERSITY SCH OF MED	26,601	SPRINGFIELD	ILLINOIS

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S07RR05845 UNIVERSITY OF TENNESSEE KNOXVILLE
   37,624    KNOXVILLE           TENNESSEE
S07RR05849 UNIVERSITY OF TEXAS AUSTIN
   29,223    AUSTIN              TEXAS
S07RR05852 TUFTS UNIVERSITY
   59,459    BOSTON              MASSACHUSETTS
S07RR05853 RIVERSIDE RESEARCH INSTITUTE
   42,605    NEW YORK            NEW YORK
S07RR05854 TEXAS AGRI AND MECH UNIV COLLEGE STATION
   23,420    COLLEGE STATION     TEXAS
S07RR05857 UNIVERSITY OF KENTUCKY
   27,241    LEXINGTON           KENTUCKY
S07RR05859 NEW YORK STATE OFFICE OF ALC AND SUB ABU
   34,038    NEW YORK            NEW YORK
S07RR05860 POPULATION COUNCIL
   50,751    NEW YORK            NEW YORK
S07RR05861 UNIVERSITY OF ILLINOIS URBANA-CHAMPAIGN
   81,327    CHAMPAIGN           ILLINOIS
S07RR05862 MEMORIAL HOSPITAL (PAWTUCKET, RI)
   39,146    PAWTUCKET           RHODE ISLAND
S07RR05863 W. ALTON JONES CELL SCIENCE CENTER
   40,898    LAKE PLACID         NEW YORK
S07RR05864 UNIVERSITY OF ILLINOIS AT CHICAGO
   25,257    CHICAGO             ILLINOIS
S07RR05865 INDIANA UNIV-PURDUE UNIV AT INDIANAPOLIS
   17,215    INDIANAPOLIS        INDIANA
S07RR05866 UNIVERSITY OF WISCONSIN MADISON
    9,756    MADISON             WISCONSIN
S07RR05867 FLORIDA AGRICULTURAL AND MECHANICAL UNIV
   34,222    TALLAHASSEE         FLORIDA
S07RR05870 MARSHALL UNIVERSITY
   22,915    HUNTINGTON          WEST VIRGINIA
S07RR05874 GRADUATE HOSPITAL (PHILADELPHIA)
   74,924    PHILADELPHIA        PENNSYLVANIA
S07RR05876 WHITTIER INSTITUTE FOR DIABETES & ENDOC
   27,081    LA JOLLA            CALIFORNIA
S07RR05877 UNIVERSITY OF IOWA
   16,510    IOWA CITY           IOWA
S07RR05878 AGOURON INSTITUTE
   28,591    LA JOLLA            CALIFORNIA
S07RR05879 TEXAS COLLEGE OF OSTEOPATHIC MEDICINE
   38,279    FORT WORTH          TEXAS
S07RR05880 J. DAVID GLADSTONE FOUNDATION
   14,881    LOS ANGELES         CALIFORNIA
S07RR05882 MEDICAL BIOLOGY INSTITUTE
   78,011    LA JOLLA            CALIFORNIA
S07RR05883 BOSTON CITY HOSPITAL
   51,573    BOSTON              MASSACHUSETTS
S07RR05886 BETH ISRAEL MEDICAL CTR (NEW YORK)
   29,877    NEW YORK            NEW YORK
S07RR05888 CHILDREN'S HOSPITAL AND HEALTH CENTER
   22,361    SAN DIEGO           CALIFORNIA
S07RR05889 BLOOD CENTER OF SOUTHEASTERN WISCONSIN
   33,649    MILWAUKEE           WISCONSIN
S07RR05890 UNIVERSITY OF COLORADO HLTH SCIENCES CTR
   18,093    DENVER              COLORADO
S07RR05893 ILLINOIS CANCER COUNCIL
   54,325    CHICAGO             ILLINOIS
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S07RR05894	AMC CANCER RESEARCH CENTER	30,472	LAKEWOOD	COLORADO
S07RR05895	FOX CHASE CANCER CENTER	68,836	PHILADELPHIA	PENNSYLVANIA
S07RR05896	UNIVERSITY OF MINNESOTA AT DULUTH	29,817	DULUTH	MINNESOTA
S07RR05897	UNIVERSITY OF TEXAS HLTH SCI CTR SAN ANT	34,569	SAN ANTONIO	TEXAS
S07RR05898	TUFTS UNIVERSITY	29,555	BOSTON	MASSACHUSETTS
S07RR05899	CHILDREN'S HOSPITAL (BOSTON)	288,794	BOSTON	MASSACHUSETTS
S07RR05903	CENTER FOR MOLECULAR MEDICINE & IMMUNOLO	35,636	NEWARK	NEW JERSEY
S07RR05905	CHILDREN'S HOSPITAL (COLUMBUS)	36,999	COLUMBUS	OHIO
S07RR05906	BAYLOR UNIVERSITY	23,139	WACO	TEXAS
S07RR05907	MOREHOUSE SCHOOL OF MEDICINE	9,292	ATLANTA	GEORGIA
S07RR05908	UNIV OF MED/DENT NJ-SCH OSTEOPATHIC MED	39,710	PISCATAWAY	NEW JERSEY
S07RR05909	RUTGERS THE STATE UNIV NEW BRUNSWICK	25,045	NEW BRUNSWICK	NEW JERSEY
S07RR05910	PURDUE UNIVERSITY WEST LAFAYETTE	17,818	WEST LAFAYETTE	INDIANA
S07RR05911	NORTH CAROLINA STATE UNIVERSITY RALEIGH	25,082	RALEIGH	NORTH CAROLINA
S07RR05912	UNIVERSITY OF WISCONSIN MADISON	43,480	MADISON	WISCONSIN
S07RR05913	UNIVERSITY OF ARIZONA	11,639	TUCSON	ARIZONA
S07RR05914	OREGON HEALTH SCIENCES UNIVERSITY	16,402	PORTLAND	OREGON
S07RR05915	BAYLOR COLLEGE OF DENTISTRY	14,844	DALLAS	TEXAS
S07RR05916	WASHINGTON UNIVERSITY	27,169	SAINT LOUIS	MISSOURI
S07RR05917	UNIVERSITY OF CALIF-LAWRNC LVRMR NAT LAB	53,182	LIVERMORE	CALIFORNIA
S07RR05918	UNIVERSITY OF CALIF-LAWRENC BERKELEY LAB	183,990	BERKELEY	CALIFORNIA
S07RR05919	UNIVERSITY OF CALIF-LOS ALAMOS NAT LAB	108,690	LOS ALAMOS	NEW MEXICO
S07RR05920	NORTHERN CALIFORNIA CANCER PROGRAM, INC.	60,180	PALO ALTO	CALIFORNIA
S07RR05922	SWEDISH HOSPITAL MEDICAL CENTER	20,216	SEATTLE	WASHINGTON
S07RR05924	NORTH SHORE UNIVERSITY HOSPITAL	18,523	MANHASSET	NEW YORK
S07RR05927	BOSTON UNIVERSITY	91,371	BOSTON	MASSACHUSETTS
S07RR05929	JOHN MUIR MEMORIAL HOSP (WALNUT CRK, CA)	36,369	WALNUT CREEK	CALIFORNIA
S07RR05930	UNIVERSITY OF MINNESOTA OF MNPLS-ST PAUL	19,161	MINNEAPOLIS	MINNESOTA
S07RR05932	PACIFIC INSTITUTE FOR RES AND EVALUATION	32,462	BETHESDA	MARYLAND

S07RR05933	UNIVERSITY OF FLORIDA	32,093	GAINESVILLE	FLORIDA
S07RR05937	WHITEHEAD INSTITUTE FOR BIOMEDICAL RES	120,268	CAMBRIDGE	MASSACHUSETTS
S07RR05938	RESEARCH INSTITUTE ON ALCOHOLISM	17,422	BUFFALO	NEW YORK
S07RR05939	ISSAQUAH HEALTH RESEARCH INSTITUTE	24,273	ISSAQUAH	WASHINGTON
S07RR05942	UNIVERSITY OF NEBRASKA MEDICAL CENTER	10,487	OMAHA	NEBRASKA
S07RR05943	UNIVERSITY OF FLORIDA	16,737	GAINESVILLE	FLORIDA
S07RR05944	OHIO STATE UNIVERSITY	15,034	COLUMBUS	OHIO
S07RR05947	CASE WESTERN RESERVE UNIVERSITY	18,868	CLEVELAND	OHIO
S07RR05949	UNIVERSITY OF MISSOURI COLUMBIA	18,260	COLUMBIA	MISSOURI
S07RR05950	BRIGHAM AND WOMEN'S HOSPITAL	309,669	BOSTON	MASSACHUSETTS
S07RR05951	JAMES N. GAMBLE INSTITUTE OF MEDICAL RES	16,951	CINCINNATI	OHIO
S07RR05952	UNIVERSITY OF ROCHESTER	12,357	ROCHESTER	NEW YORK
S07RR05953	NORTHWESTERN MEMORIAL HOSPITAL	32,450	CHICAGO	ILLINOIS
S07RR05954	UNIVERSITY OF WISCONSIN MADISON	36,686	MADISON	WISCONSIN
S07RR05955	NEWARK BETH ISRAEL MEDICAL CENTER	13,385	NEWARK	NEW JERSEY
S07RR05956	CANCER THERAPY AND RESEARCH CENTER	56,796	SAN ANTONIO, TX	
S07RR05957	VIRGINIA POLYTECHNIC INST AND ST UNIV	24,586	BLACKSBURG	VIRGINIA
S07RR05958	UNIVERSITY OF TEXAS HLTH CTR AT TYLER	44,981	TYLER	TEXAS
S07RR05959	EAST TENNESSEE STATE UNIVERSITY	13,139	JOHNSON CITY	TENNESSEE
S07RR05960	MARSHFIELD MEDICAL FOUNDATION	14,932	MARSHFIELD	WISCONSIN
S07RR05961	SHOWA UNIVERSITY RES INST/BIOMED IN FLA	28,598	SAINT PETERSBURG	FLORIDA
S07RR05962	INDIANA UNIVERSITY BLOOMINGTON	11,515	BLOOMINGTON	INDIANA
S07RR05963	MERCER UNIVERSITY MACON	9,705	MACON	GEORGIA
S07RR05964	ELEANOR ROOSEVELT INST FOR CANCER RES	34,777	DENVER	COLORADO
S07RR05965	UNIVERSITY OF PITTSBURGH	17,047	PITTSBURGH	PENNSYLVANIA
S07RR05966	CALIFORNIA PUBLIC HEALTH FOUNDATION	15,420	BERKELEY	CALIFORNIA
S07RR05967	UNIVERSITY OF NORTH CAROLINA CHAPEL HILL	18,548	CHAPEL HILL	NORTH CAROLINA
S07RR05968	UNIVERSITY OF ALABAMA AT BIRMINGHAM	49,457	BIRMINGHAM	ALABAMA
S07RR05969	OHIO STATE UNIVERSITY	9,923	COLUMBUS	OHIO

S07RR05970	UNIVERSITY OF TEXAS	13,823	HOUSTON, TX	
S07RR07002	UNIVERSITY OF ARIZONA	156,353	TUCSON	ARIZONA
S07RR07003	CALIFORNIA INSTITUTE OF TECHNOLOGY	224,492	PASADENA	CALIFORNIA
S07RR07004	SAN DIEGO STATE UNIVERSITY	57,197	SAN DIEGO	CALIFORNIA
S07RR07005	STANFORD UNIVERSITY	250,980	STANFORD	CALIFORNIA
S07RR07006	UNIVERSITY OF CALIFORNIA BERKELEY	300,314	BERKELEY	CALIFORNIA
S07RR07007	UNIVERSITY OF CALIFORNIA DAVIS	164,272	DAVIS	CALIFORNIA
S07RR07008	UNIVERSITY OF CALIFORNIA IRVINE	162,639	IRVINE	CALIFORNIA
S07RR07009	UNIVERSITY OF CALIFORNIA LOS ANGELES	284,232	LOS ANGELES	CALIFORNIA
S07RR07010	UNIVERSITY OF CALIFORNIA RIVERSIDE	100,901	RIVERSIDE	CALIFORNIA
S07RR07011	UNIVERSITY OF CALIFORNIA SAN DIEGO	248,895	LA JOLLA	CALIFORNIA
S07RR07012	UNIVERSITY OF SOUTHERN CALIFORNIA	152,903	LOS ANGELES	CALIFORNIA
S07RR07013	UNIVERSITY OF COLORADO AT BOULDER	220,689	BOULDER	COLORADO
S07RR07014	UNIVERSITY OF CONNECTICUT STORRS	126,456	STORRS	CONNECTICUT
S07RR07015	YALE UNIVERSITY	263,929	NEW HAVEN	CONNECTICUT
S07RR07016	UNIVERSITY OF DELAWARE	65,359	NEWARK	DELAWARE
S07RR07019	GEORGE WASHINGTON UNIVERSITY	21,331	WASHINGTON	DIST OF COL
S07RR07020	FLORIDA STATE UNIVERSITY	93,211	TALLAHASSEE	FLORIDA
S07RR07021	UNIVERSITY OF FLORIDA	95,974	GAINESVILLE	FLORIDA
S07RR07022	UNIVERSITY OF MIAMI	35,687	CORAL GABLES	FLORIDA
S07RR07023	EMORY UNIVERSITY	104,707	ATLANTA	GEORGIA
S07RR07024	GEORGIA INSTITUTE OF TECHNOLOGY	69,123	ATLANTA	GEORGIA
S07RR07025	UNIVERSITY OF GEORGIA	142,178	ATHENS	GEORGIA
S07RR07026	UNIVERSITY OF HAWAII AT MANOA	116,919	HONOLULU	HAWAII
S07RR07027	ILLINOIS INSTITUTE OF TECHNOLOGY	31,538	CHICAGO	ILLINOIS
S07RR07028	NORTHWESTERN UNIVERSITY	187,154	EVANSTON	ILLINOIS
S07RR07029	UNIVERSITY OF CHICAGO	104,395	CHICAGO	ILLINOIS
S07RR07030	UNIVERSITY OF ILLINOIS URBANA-CHAMPAIGN	241,375	CHAMPAIGN	ILLINOIS
S07RR07031	INDIANA UNIVERSITY BLOOMINGTON	160,316	BLOOMINGTON	INDIANA

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S07RR07032 PURDUE UNIVERSITY WEST LAFAYETTE
  212,357    WEST LAFAYETTE     INDIANA
S07RR07033 UNIVERSITY OF NOTRE DAME
  81,064     NOTRE DAME         INDIANA
S07RR07034 IOWA STATE UNIVERSITY OF SCIENCE & TECH
  67,282     AMES               IOWA
S07RR07035 UNIVERSITY OF IOWA
  152,962    IOWA CITY          IOWA
S07RR07036 KANSAS STATE UNIVERSITY
  67,142     MANHATTAN          KANSAS
S07RR07037 UNIVERSITY OF KANSAS LAWRENCE
  119,127    LAWRENCE           KANSAS
S07RR07039 LOUISIANA STATE UNIV A&M COL BATON ROUGE
  56,682     BATON ROUGE        LOUISIANA
S07RR07040 TULANE UNIVERSITY OF LOUISIANA
  75,362     NEW ORLEANS        LOUISIANA
S07RR07041 JOHNS HOPKINS UNIVERSITY
  176,864    BALTIMORE          MARYLAND
S07RR07042 UNIVERSITY OF MARYLAND COLLEGE PK CAMPUS
  98,340     COLLEGE PARK       MARYLAND
S07RR07043 BOSTON UNIVERSITY
  100,588    BOSTON             MASSACHUSETTS
S07RR07044 BRANDEIS UNIVERSITY
  185,664    WALTHAM            MASSACHUSETTS
S07RR07046 HARVARD UNIVERSITY
  273,984    CAMBRIDGE          MASSACHUSETTS
S07RR07047 MASSACHUSETTS INSTITUTE OF TECHNOLOGY
  315,704    CAMBRIDGE          MASSACHUSETTS
S07RR07048 UNIVERSITY OF MASSACHUSETTS AMHERST
  101,334    AMHERST            MASSACHUSETTS
S07RR07049 MICHIGAN STATE UNIVERSITY
  129,484    EAST LANSING       MICHIGAN
S07RR07050 UNIVERSITY OF MICHIGAN AT ANN ARBOR
  243,697    ANN ARBOR          MICHIGAN
S07RR07051 WAYNE STATE UNIVERSITY
  94,475     DETROIT            MICHIGAN
S07RR07052 UNIVERSITY OF MINNESOTA OF MNPLS-ST PAUL
  177,668    MINNEAPOLIS        MINNESOTA
S07RR07053 UNIVERSITY OF MISSOURI COLUMBIA
  93,372     COLUMBIA           MISSOURI
S07RR07054 WASHINGTON UNIVERSITY
  143,821    SAINT LOUIS        MISSOURI
S07RR07055 UNIVERSITY OF NEBRASKA LINCOLN
  49,763     LINCOLN            NEBRASKA
S07RR07056 DARTMOUTH COLLEGE
  33,124     HANOVER            NEW HAMPSHIRE
S07RR07057 PRINCETON UNIVERSITY
  177,781    PRINCETON          NEW JERSEY
S07RR07058 RUTGERS THE STATE UNIV NEW BRUNSWICK
  183,870    NEW BRUNSWICK      NEW JERSEY
S07RR07059 RUTGERS THE STATE UNIV NEWARK
  39,258     NEWARK             NEW JERSEY
S07RR07060 COLUMBIA UNIVERSITY NEW YORK
  249,966    NEW YORK           NEW YORK
S07RR07061 CORNELL UNIVERSITY ITHACA
  283,203    ITHACA             NEW YORK
S07RR07062 NEW YORK UNIVERSITY
  72,704     NEW YORK           NEW YORK
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S07RR07064	QUEENS COLLEGE	20,835	NEW YORK	NEW YORK
S07RR07065	ROCKEFELLER UNIVERSITY	303,307	NEW YORK	NEW YORK
S07RR07066	STATE UNIVERSITY OF NEW YORK AT BUFFALO	68,212	BUFFALO	NEW YORK
S07RR07067	STATE UNIVERSITY NEW YORK STONY BROOK	156,828	STONY BROOK	NEW YORK
S07RR07068	SYRACUSE UNIVERSITY AT SYRACUSE	135,042	SYRACUSE	NEW YORK
S07RR07069	UNIVERSITY OF ROCHESTER	167,025	ROCHESTER	NEW YORK
S07RR07070	DUKE UNIVERSITY	114,432	DURHAM	NORTH CAROLINA
S07RR07071	NORTH CAROLINA STATE UNIVERSITY RALEIGH	79,584	RALEIGH	NORTH CAROLINA
S07RR07072	UNIVERSITY OF NORTH CAROLINA CHAPEL HILL	153,007	CHAPEL HILL	NORTH CAROLINA
S07RR07074	OHIO STATE UNIVERSITY	137,864	COLUMBUS	OHIO
S07RR07075	UNIVERSITY OF CINCINNATI	41,351	CINCINNATI	OHIO
S07RR07077	OKLAHOMA STATE UNIVERSITY STILLWATER	13,312	STILLWATER	OKLAHOMA
S07RR07078	UNIVERSITY OF OKLAHOMA NORMAN	60,645	NORMAN	OKLAHOMA
S07RR07079	OREGON STATE UNIVERSITY	145,258	CORVALLIS	OREGON
S07RR07080	UNIVERSITY OF OREGON	152,653	EUGENE	OREGON
S07RR07081	CARNEGIE-MELLON UNIVERSITY	143,051	PITTSBURGH	PENNSYLVANIA
S07RR07082	PENNSYLVANIA STATE UNIVERSITY PARK	190,523	UNIVERSITY PARK	PENNSYLVANIA
S07RR07083	UNIVERSITY OF PENNSYLVANIA	216,923	PHILADELPHIA	PENNSYLVANIA
S07RR07084	UNIVERSITY OF PITTSBURGH	156,313	PITTSBURGH	PENNSYLVANIA
S07RR07085	BROWN UNIVERSITY	83,125	PROVIDENCE	RHODE ISLAND
S07RR07086	UNIVERSITY OF RHODE ISLAND	32,501	KINGSTON	RHODE ISLAND
S07RR07088	UNIVERSITY OF TENNESSEE KNOXVILLE	73,902	KNOXVILLE	TENNESSEE
S07RR07090	TEXAS AGRI AND MECH UNIV COLLEGE STATION	101,277	COLLEGE STATION	TEXAS
S07RR07091	UNIVERSITY OF TEXAS AUSTIN	186,758	AUSTIN	TEXAS
S07RR07092	UNIVERSITY OF UTAH	152,962	SALT LAKE CITY	UTAH
S07RR07093	UTAH STATE UNIVERSITY	21,447	LOGAN	UTAH
S07RR07094	UNIVERSITY OF VIRGINIA CHARLOTTESVILLE	136,925	CHARLOTTESVILLE	VIRGINIA
S07RR07095	VIRGINIA POLYTECHNIC INST AND ST UNIV	55,702	BLACKSBURG	VIRGINIA
S07RR07096	UNIVERSITY OF WASHINGTON	220,392	SEATTLE	WASHINGTON

S07RR07097	WASHINGTON STATE UNIVERSITY	85,644	PULLMAN	WASHINGTON
S07RR07098	UNIVERSITY OF WISCONSIN MADISON	291,731	MADISON	WISCONSIN
S07RR07099	UNIVERSITY OF CALIFORNIA SANTA BARBARA	125,927	SANTA BARBARA	CALIFORNIA
S07RR07100	MONTANA STATE UNIVERSITY	35,942	BOZEMAN	MONTANA
S07RR07101	UNIVERSITY OF ARKANSAS AT FAYETTEVILLE	15,015	FAYETTEVILLE	ARKANSAS
S07RR07103	RICE UNIVERSITY	85,999	HOUSTON	TEXAS
S07RR07104	RENSSELAER POLYTECHNIC INSTITUTE	74,942	TROY	NEW YORK
S07RR07107	WESLEYAN UNIVERSITY	39,765	MIDDLETOWN	CONNECTICUT
S07RR07108	UNIVERSITY OF NEW HAMPSHIRE	42,201	DURHAM	NEW HAMPSHIRE
S07RR07109	HUNTER COLLEGE	81,941	NEW YORK	NEW YORK
S07RR07110	AMHERST COLLEGE	12,778	AMHERST	MASSACHUSETTS
S07RR07112	ARIZONA STATE UNIVERSITY	60,328	TEMPE	ARIZONA
S07RR07113	CASE WESTERN RESERVE UNIVERSITY	152,349	CLEVELAND	OHIO
S07RR07114	UNIVERSITY OF KENTUCKY	45,800	LEXINGTON	KENTUCKY
S07RR07115	TEMPLE UNIVERSITY	39,226	PHILADELPHIA	PENNSYLVANIA
S07RR07117	HOWARD UNIVERSITY	58,345	WASHINGTON	DIST OF COL
S07RR07118	SOUTHERN ILLINOIS UNIVERSITY CARBONDALE	50,352	CARBONDALE	ILLINOIS
S07RR07119	BROOKLYN COLLEGE	24,875	NEW YORK	NEW YORK
S07RR07120	SAN FRANCISCO STATE UNIVERSITY	13,330	SAN FRANCISCO	CALIFORNIA
S07RR07121	UNIVERSITY OF SOUTH FLORIDA	27,211	TAMPA	FLORIDA
S07RR07122	STATE UNIVERSITY OF NEW YORK AT ALBANY	110,993	ALBANY	NEW YORK
S07RR07123	CATHOLIC UNIVERSITY OF AMERICA	15,260	WASHINGTON	DIST OF COL
S07RR07125	UNIVERSITY OF VERMONT & ST AGRIC COLLEGE	45,819	BURLINGTON	VERMONT
S07RR07127	COLORADO STATE UNIVERSITY	76,161	FORT COLLINS	COLORADO
S07RR07128	PORTLAND STATE UNIVERSITY	17,976	PORTLAND	OREGON
S07RR07129	DREXEL UNIVERSITY	37,864	PHILADELPHIA	PENNSYLVANIA
S07RR07131	OAKLAND UNIVERSITY	51,123	ROCHESTER	MICHIGAN
S07RR07132	CITY COLLEGE OF NEW YORK	65,452	NEW YORK	NEW YORK
S07RR07133	UNIVERSITY OF TEXAS DALLAS	58,428	RICHARDSON	TEXAS

S07RR07135	UNIVERSITY OF CALIFORNIA SANTA CRUZ	88,538	SANTA CRUZ	CALIFORNIA
S07RR07136	GEORGETOWN UNIVERSITY	57,176	WASHINGTON	DIST OF COL
S07RR07138	UNIVERSITY OF DENVER	54,085	DENVER	COLORADO
S07RR07143	NORTHEASTERN UNIVERSITY	43,634	BOSTON	MASSACHUSETTS
S07RR07147	UNIVERSITY OF HOUSTON-UNIVERSITY PARK	79,994	HOUSTON	TEXAS
S07RR07148	UNIVERSITY OF TEXAS HLTH SCI CTR HOUSTON	64,931	HOUSTON	TEXAS
S07RR07149	STATE UNIVERSITY NEW YORK BINGHAMTON	34,338	BINGHAMTON	NEW YORK
S07RR07150	FORDHAM UNIVERSITY	41,263	NEW YORK	NEW YORK
S07RR07151	UNIVERSITY OF ALABAMA IN UNIVERSITY	29,694	UNIVERSITY	ALABAMA
S07RR07153	UNIVERSITY OF LOUISVILLE	15,021	LOUISVILLE	KENTUCKY
S07RR07154	NEW MEXICO STATE UNIVERSITY LAS CRUCES	21,886	LAS CRUCES	NEW MEXICO
S07RR07155	WRIGHT STATE UNIVERSITY	9,578	DAYTON	OHIO
S07RR07156	BOSTON COLLEGE	31,924	NEWTON	MASSACHUSETTS
S07RR07157	UNIVERSITY OF WYOMING	25,796	LARAMIE	WYOMING
S07RR07158	UNIVERSITY OF ILLINOIS AT CHICAGO	104,764	CHICAGO	ILLINOIS
S07RR07159	UNIVERSITY OF MARYLAND BALT CO CAMPUS	66,163	CATONSVILLE	MARYLAND
S07RR07160	UNIVERSITY OF SOUTH CAROLINA AT COLUMBIA	121,342	COLUMBIA	SOUTH CAROLINA
S07RR07161	UNIVERSITY OF MAINE AT ORONO	17,445	ORONO	MAINE
S07RR07167	MEHARRY MEDICAL COLLEGE	28,962	NASHVILLE	TENNESSEE
S07RR07168	REED COLLEGE	16,480	PORTLAND	OREGON
S07RR07170	UNIVERSITY OF IDAHO	20,071	MOSCOW	IDAHO
S07RR07171	GEORGIA STATE UNIVERSITY	16,382	ATLANTA	GEORGIA
S07RR07173	LEHIGH UNIVERSITY	20,095	BETHLEHEM	PENNSYLVANIA
S07RR07175	UNIVERSITY OF TEXAS HLTH SCI CTR DALLAS	285,011	DALLAS	TEXAS
S07RR07176	NORTHERN ILLINOIS UNIVERSITY	26,944	DE KALB	ILLINOIS
S07RR07178	UNIVERSITY OF ALABAMA AT BIRMINGHAM	33,970	BIRMINGHAM	ALABAMA
S07RR07179	TUFTS UNIVERSITY	83,285	MEDFORD	MASSACHUSETTS
S07RR07181	UNIVERSITY OF WISCONSIN MILWAUKEE	14,769	MILWAUKEE	WISCONSIN
S07RR07183	TEXAS TECH UNIVERSITY	16,652	LUBBOCK	TEXAS

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S07RR07184 OREGON GRADUATE CTR STUDY AND RESEARCH
   29,754    BEAVERTON           OREGON
S07RR07185 UNIVERSITY OF NEW MEXICO ALBUQUERQUE
   32,489    ALBUQUERQUE         NEW MEXICO
S07RR07186 WELLESLEY COLLEGE
   13,776    WELLESLEY           MASSACHUSETTS
S07RR07187 UNIVERSITY OF TEXAS HLTH SCI CTR SAN ANT
  194,356    SAN ANTONIO         TEXAS
S07RR07189 OHIO UNIVERSITY ATHENS
   11,683    ATHENS              OHIO
S07RR07190 FLORIDA INSTITUTE OF TECHNOLOGY
    8,569    MELBOURNE           FLORIDA
S07RR07192 BOWLING GREEN STATE UNIV BOWLING GREEN
   17,047    BOWLING GREEN       OHIO
S07RR07194 SOUTHERN METHODIST UNIVERSITY
   16,939    DALLAS              TEXAS
S07RR07195 NORTH TEXAS STATE UNIVERSITY
   33,977    DENTON              TEXAS
S07RR07196 MARQUETTE UNIVERSITY
   12,128    MILWAUKEE           WISCONSIN
S07RR07199 UNIVERSITY OF MASSACHUSETTS BOSTON
   24,602    BOSTON              MASSACHUSETTS
S07RR07201 VANDERBILT UNIVERSITY
  142,530    NASHVILLE           TENNESSEE
S07RR07204 VIRGINIA COMMONWEALTH UNIVERSITY
   29,411    RICHMOND            VIRGINIA
S07RR07205 UNIVERSITY OF TEXAS MED BR GALVESTON
  136,695    GALVESTON           TEXAS
S07RR07206 NORTH DAKOTA STATE UNIVERSITY
    8,513    FARGO               NORTH DAKOTA
S07RR07208 KENT STATE UNIVERSITY AT KENT
   13,173    KENT                OHIO
S07RR07210 LOYOLA UNIVERSITY OF CHICAGO
   17,617    CHICAGO             ILLINOIS
S07RR07216 UNIVERSITY OF NEBRASKA MEDICAL CENTER
   79,539    OMAHA               NEBRASKA
S07RR07217 UNIVERSITY OF TEXAS SAN ANTONIO
   33,208    SAN ANTONIO         TEXAS
S07RR07220 UNIVERSITY OF NEVADA RENO
   16,209    RENO                NEVADA
S07RR07226 UNIVERSITY OF PUERTO RICO MED SCIENCES
   42,569    SAN JUAN            PUERTO RICO
S07RR07227 INDIANA UNIV-PURDUE UNIV AT INDIANAPOLIS
    9,650    INDIANAPOLIS        INDIANA
S07RR07228 GEORGE MASON UNIVERSITY
    8,278    FAIRFAX             VIRGINIA
S07RR07229 MEMPHIS STATE UNIVERSITY
   24,862    MEMPHIS             TENNESSEE
S07RR07230 WAKE FOREST UNIVERSITY
   12,925    WINSTON-SALEM       NORTH CAROLINA
S07RR07231 POLYTECHNIC INSTITUTE OF NEW YORK
   13,075    NEW YORK            NEW YORK

    $59,460,571 AWARDED TO 575 RECIPIENTS
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TERMINATION OF THE BRSG PROGRAM

Mr. NATCHER. Last year you told us that the biomedical research support grants were used as follows: 35 percent for pilot research projects, 32 percent for regular research projects, 27 percent for central research facilities, and 6 percent for other research activities.

Are there other funds in the NIH budget which can be used for research institutions for these purposes if the biomedical research support grant is terminated?

Dr. PICKETT. There are other funds for shared resources, for example, in the shared instrumentation grant program, and in the center grants that we provide through the three centers programs, clinical research, biomedical research technology and animal resources.

Pilot research can be supported through new investigator grants, research career development awards and probably through individual research fellowships and postdoctoral traineeships.

The unique characteristic of the formula grant is the flexible local allocation of funds, different from categorical, individual research project grants, so the answer is both yes and no, Mr. Natcher.

While there are places—grant programs—where you can get this kind of thing, the flexible allocation characteristic is unique to the biomedical research support grant.

Mr. NATCHER. If the biomedical research support grant is terminated, how will research institutions make up for the loss of funds?

Dr. PICKETT. Research institutions will need to use more of their own resources for these purposes. They will need to maximize their capacity to attract local, state and private sources of funds for these purposes.

Mr. NATCHER. At what level, Dr. Pickett, was the decision made to terminate this program, NIH? The Public Health Service, OMB? What level, Doctor?

Dr. PICKETT. I believe the decision was made at NIH, on the basis that in a time when top priority is put on the individual research project grant which is focused on a specific program area, that valuable as it is, this generalized institutional support had to take a lower priority, and be eliminated. I believe that was the basis on which the decision was made, and I believe the decision was made at NIH, at a level above mine.

BRS PROGRAM EVALUATION

Mr. NATCHER. Last year you told us about the results of the evaluation of the biomedical research support program conducted in 1984. We will insert your response in the record at this point.

[The information follows:]

EVALUATION OF BRSG PROGRAM

An evaluation study of the Biomedical Research Support Grant (BRSG) Program was conducted in 1984 by Aurora Associates, Inc., of Washington, D.C. This study concluded that:

- Program format is consistent with and supports the attainment of Program objectives.
- The BRSG Program's emphasis on decentralized decision-making allows institutions to target resources to areas that contribute to institutional research and development strategies.
- BRSG funds are highly coveted by investigators and administrators because of their flexibility and the institution's ability to administer them on a quick-turnaround basis.
- The BRSG Program generally is administered with a high degree of rigor and formality in the institutions, possibly because the funds are valued and seriously competed for by investigators and programs within the institution.
- BRSG Program funds are reaching the programs, departments, and investigators for which they are intended, and as far as this study can judge, are resulting in impressive benefits.
- No evidence was found to suggest that a more restrictive definition of BRSG fund usage would increase Program performance; if anything, the results suggest that increased restrictiveness could be counter-productive.
- Little, if any, program or cost benefit would be derived from increasing or greatly modifying requirements for monitoring grantee institutions.

This study reaffirms the value and benefits of the Biomedical Research Support Grant to both the grantee institutions and the research programs of the Public Health Service.

Mr. NATCHER. Have there been any further evaluations of the program, and if so, what are the findings, Dr. Pickett?

Dr. PICKETT. There has not been an evaluation of the program since that, the one you speak of, which was conducted two years ago.

Mr. NATCHER. 1984?

Dr. PICKETT. No, there has not been another evaluation since that time.

RESEARCH INSTRUMENTATION

Mr. NATCHER. Your budget includes $31,808,000 for shared instrumentation grants. How much of the total NIH budget do you estimate will be used for research equipment and if you will, give us a breakdown for the record.

Dr. PICKETT. The current estimate for research equipment at NIH, as a percent of the total extramural research budget, is 4.2 percent.

Mr. NATCHER. All right, are we keeping up with need for new and replaced equipment?

Dr. PICKETT. It depends on whom you listen to. We participated in providing support for a survey of research equipment needs in universities. We participated with the NSF in a lengthy study of this kind.

The data were gathered in 1983 and reported to us just about one year ago, so for what they are worth—they may need to be updated at this point—of the Department Chairmen in biological and medical science's departments who participated, nearly 60 percent reported that there are important areas that cannot be addressed because of lack of necessary equipment.

PRIMATE RESEARCH CENTERS

Mr. NATCHER. Dr. Pickett, your 1987 budget includes $23,344,000 for the seven regional primate centers. How long have we been supporting these centers?

Dr. PICKETT. Since, I believe, 1962.

Mr. NATCHER. If you will insert in the record a list of the centers along with the most recent funding for each one.

[The information follows:]

REGIONAL PRIMATE RESEARCH CENTERS - FY 1985

Grant No.	Name of Institution City, State	1985 Actual Award
P51RR00163	Medical Research Foundation of Oregon Oregon Primate Research Center Beaverton, Oregon	$4,354,071
P51RR00164	Tulane University of Louisiana Delta Primate Research Center Covington, Louisiana	2,837,411
P51RR00165	Emory University Yerkes Regional Primate Research Center Atlanta, Georgia	3,370,554
P51RR00166	University of Washington Regional Primate Research Center Seattle, Washington	3,991,849
P51RR00167	University of Wisconsin Madison Wisconsin Primate Research Center Madison, Wisconsin	3,221,859
P51RR00168	Harvard University New England Regional Primate Research Center Southborough, Massachusetts	3,309,494
P51RR00169	University of California Davis California Primate Research Center Davis, California	3,175,762
	Total:	24,261,000

QUALITY OF RESEARCH AT THE PRIMATE CENTERS

Mr. NATCHER. Last week, Dr. Pickett, a witness for the Humane Society told us that the primate centers are characterized by poor quality research, inadequate care of their animals and a waste of almost scarce biomedical research funds.

What do you say to a charge like that, Dr. Pickett?

Dr. PICKETT. Well, I would term those charges false. All of the centers are very well run. Six of them are accredited by the American Association for the Accreditation of Laboratory Animal Care, and the seventh one is well on its way to proper accreditation.

The quality of the research cannot be characterized as worthless, useless or very bad.

The core staff must have research grants funded by NIH, and knowing what we know about the stringency of priority cutoffs at this time, everyone is doing excellent work.

The third charge was it is a great waste of money. I don't think so. The research findings from the primate centers, in infectious disease, neuroscience, hearing, neurosurgery, so forth, which we have described here and some of which are described in our long statement, prove that these centers are not a waste of Federal monies.

Last year I talked about monkey work that led directly into some human work in sickle-cell anemia in the Boston area; and scientists at the California Center this year, for example, have developed a vaccine that seems to be very effective in challenging SAIDS—an immune deficiency syndrome in primates similar to the human disease—and in teaching us a lot about the disease.

No, I cannot possibly subscribe to those charges.

The evidence is ample against them.

Mr. NATCHER. All right, Dr. Pickett, are the research programs of the primate centers subjected to outside review, or evaluation for scientific merit?

Dr. PICKETT. Yes, they are. Each primate center must compete for its core support, roughly every five years.

The site visits are extremely searching, very complex, and very critical.

The review by the Review Committee, to which the site visitors report, is incisive and critical. The applications are enormous and very complicated and are looked at in detail by the National Advisory Research Resources Council. Yes, they are subjected to sharp, critical outside peer review at two levels, just like anything else NIH supports.

Mr. NATCHER. With the $23 million a year we are spending on primate centers, could it be better used for something else?

Dr. PICKETT. Could it be better used for something else?

I don't think so. When I think about the fact that the chimpanzee, for example, is the only animal besides man that is known to develop antibodies to the virus that causes AIDS in humans and the potential that has for vaccine development for the human illness, I cannot agree that they should be used for something else. That is a very unique possibility.

ANIMAL FACILITY IMPROVEMENTS

Mr. Natcher. As you know, public concern about the treatment of animals used in biomedical research is growing. Your 1987 budget contains $1 million for repair and renovation needs of primate centers, and $3,981,000 for animal facilities improvement grants.

Do you have a backlog, Dr. Pickett, of approved requests for grants for improvements to animal facilities?

Dr. Pickett. The new program I mentioned, which was launched in 1985, elicited 100 applications from the research community for funds to repair and replace essential cage-washing equipment, modify animal quarters, make more suitable spaces for the animals and so forth. We were able to fund 23 of those approved requests out of 1985 funds.

The funds available in 1986 will enable us to fund approximately the next nine applications, and in 1987, we will be able to fund nine more. There were 74 applications approved out of that set of 100 applications. We funded 23 of those applications in 1985 and have since received 2 additional applications leading 53 approved unfunded applications in 1986.

Mr. Natcher. What is the dollar amount, Dr. Pickett, of the backlog?

Dr. Pickett. Those 53 approved unfunded applications have requested a total of $18.7 million.

Mr. Natcher. Mr. Conte, I yield to you.

BRSG PROGRAM

Mr. Conte. Doctor Pickett, it is good to have you before the Subcommittee again. Your budget is taking quite a hit in fiscal year 1987, bigger than even the Cancer Institute which is four times your size. I can assure you we will be taking a good look at this request.

You and I have talked in the past about the Biomedical Research Support Grant Program. Which institutions use this support mechanism the most; smaller ones with little history of NIH support, or larger, more research-intensive institutions?

Dr. Pickett. It is available to those institutions that have at least $200,000—there must be at least three eligible grants, and those are small institutions, typically your dental schools, nursing schools, and goes all the way up to the giant institutions.

They all use it, and in their annual reports comment repeatedly on the extreme value of this kind of flexible money, Mr. Conte.

Mr. Conte. Either way, Doctor, do you think this program still lays the groundwork for fostering new ideas and bringing in new researchers to the field of biomedical research?

Dr. Pickett. Yes, I do.

Mr. Conte. How many institutions received support in fiscal year 1985, and how many will get it in fiscal year 1986?

Dr. Pickett. Five hundred seventy-five in 1986, and fiscal year 1985 is 557.

Mr. Conte. What is the average award made under the program?

Dr. Pickett. $103,000 in 1986, $112,000 in 1985.

RESEARCH CENTERS AT MINORITY INSTITUTIONS

Mr. Conte. The Division of Research Resources, I believe, administers the program funded in the Office of the Director, initiated in fiscal year 1985, to establish research centers in predominantly minority institutions.

How was that $5 million awarded in fiscal year 1985?

Dr. Pickett. In fiscal year 1985 we made seven awards under the program for a total cost of $4,771,111, to three medical schools, one pharmacy school, and three graduate schools.

Mr. Conte. Put those in the record.

[The information follows:]

RESEARCH CENTERS AT MINORITY INSTITUTIONS—FY 1985

Grant No	Names of Institution, City, State	Amount
G12RR03020	Florida A&M Unviersity; Florida A&M University Research Center, Tallahassee, FL	$1,000,000
G12RR03032	Meharry Medical College; Research Infrastructure for Scientific Excellence, Nashville, TN	865,573
G12RR03037	Hunter College of CUNY, Research Center for Gene Structure and Function, New York, NY	500,000
G12RR03048	Howard University, Howard University RCMI Interdisciplinary Program, Washington, DC	646,014
G12RR03050	Ponce School of Medicine, Ponce School of Medicine Research Center, Ponce, PR	428,142
G12RR03060	CUNY City College of New York; Cellular/Molecular Basis of Development; Research Center, New York, NY	500,000 500,000
G12RR03062	Atlanta University, Atlanta University Biomedical Science Development, Atlanta, GA	831,382
Total		4,771,111

Mr. Conte. What was the average size of the grants awarded, and for how many years is the award made?

Dr. Pickett. The average size of a grant was $682,000. They range from around $428,000 to a million dollars.

Mr. Conte. For how many years is the award made?

Dr. Pickett. Five years.

Mr. Conte. In fiscal year 1986 we continued the program, and added another $5 million, which has been proposed for rescission. Without that $5 million, would there be any funding for new awards in fiscal year 1986?

Dr. Pickett. No, there will not.

Mr. Conte. Do you have any applications that have been reviewed and approved to make new awards in fiscal year 1986 if the rescission is not approved?

Dr. Pickett. Yes, sir, we have nine approved unfunded applications.

Mr. Conte. Tell us, Doctor, what do you think this program is going to accomplish, anything?

Dr. Pickett. I am very optimistic about it.

The purpose of it is to attempt to provide human and physical resources to give these institutions a step up, and to become more skilled in certain areas of science. They took it very seriously, and among the funded applications, for example, one is to become a center for neuroscience. They are using the money to equip their labs and to hire five faculty, well-trained principally in neurosciences.

Two other centers want to become very good in molecular biology. They are expanding their staffs and equipment in that area. A couple are doing major renovations in their animal facilities and buying equipment. One is building a clinical research facility so that the pharmacological research they do can be expanded into the clinical area.

Howard University is setting up an immunogenetics lab and a biostatistical service; they are all a little bit different. If all goes well, these institutions will take a step up in areas they determine they need, and that were viewed very favorably by the ad hoc review committee that was set up to deal with this program.

Mr. CONTE. I know my friends at Morehouse, are waiting for you to act on that money. What about some other schools? What is Meharry Medical School doing?

Dr. PICKETT. They are hiring five neuroscientists, using some of the funds for startups and renovating the animal facility, electron microscopy facility, studying post-stroke management; and setting up an office of research support services to enable them to submit their applications in a much more professional manner, as a major institution would.

DRR'S ROLE IN AIDS RESEARCH

Mr. CONTE. What role does the Division of Research Resources play in the total NIH battle against the AIDS virus?

Dr. PICKETT. Last year we spent $2.8 million on AIDS research. Eighteen of the general clinical research centers have AIDS patients that they are treating, studying, evaluating and at least a couple of those centers will participate in some of the new clinical trials that the NIAID will launch this year.

The primate centers are spending considerable effort on SAIDS, simian acquired immune deficiency syndrome, which has been responsible for the deaths of some 500 animals in our colonies.

Mr. CONTE. Where were these deaths taking place?

Dr. PICKETT. Around the country. Some were at Davis. I don't think any were at Wisconsin.

They are working on trying to develop vaccines, anti-virals.

They are looking at the management of these disorders, and at Yerkes, where the chimpanzee colony lives, they are looking at transmission patterns. They are looking to see whether cage mates are susceptible to transmission of the disease to animals of neighboring cages through what we call casual transmission; not through the methods that are best known for the transmission of the virus.

Mr. CONTE. You don't mean chimpanzees in separate cages, alone, do you?

Dr. PICKETT. They are looking at that and watching very carefully.

Mr. CONTE. That is interesting.

Dr. PICKETT. It would be. That is some work that is being done in cooperation with the CDC.

CLINICAL TESTING OF NEW DRUGS AND THERAPIES

Mr. CONTE. One animal in a cage and another animal in another cage near each other.

Your justifications show a decrease of two clinical research center awards in fiscal year 1987. What effect will this have on our ability to test the effectiveness of new drugs and therapies, not only for AIDS but for other diseases as well?

Dr. Pickett. It will mean that for those trials and tests to be carried out, the bed resources and so forth will have to be provided through other sources of funding, which could be research grants under which most of these people are conducting their activities. We just pay for the beds and nurses. They have to pay the salaries and so forth of the researchers.

Mr. Conte. Do these clinical centers also provide opportunities for new drug trials from the private sector?

Dr. Pickett. Yes, they do, some do work with pharmaceuticals.

Mr. Conte. Are you reimbursed for this?

Dr. Pickett. Yes, we are.

BIOLOGICAL MODELS AND MATERIALS RESOURCES SECTION

Mr. Conte. Doctor, I was interested to see that the Division created a new section on Biological Models and Materials Resources. What is the purpose of this new section?

Dr. Pickett. The Biological Models and Materials Resources section was set up in February of 1985, to develop and support cell systems, lower organisms and nonbiological models that are critically important resources to the biomedical community that are not already being supplied by the categorical institutes.

These would be cell resources, and certain kinds of lower forms of life such as the round worm nematode—*caenorhabditis elegans*—a very useful animal, has very few cells, and has been very much studied, a very, very simple basic system from which one can learn a great deal about development and activity.

We are supporting right now through that Section one major project that had been supported by central NIH that was passed over to DRR, the American Type Culture Collection, a repository for research located here in this area. We are also supporting a major cell resource center at MIT and partly supporting that roundworm resource with the aging institute. Something funny happens at the very end of its life that looks like speeded up aging. We give partial support to a tissue exchange, the National Diabetes Research Interchange, which is supported by several institutes at NIH.

Also in that Section, we are following up the recommendations of that major study by the National Academy of Sciences; *Models for Biomedical Research. A New Perspective.*

The report made a number of recommendations including that we should make appropriate systems available to the research community like cell banks, stock centers for mutant strains, cell lines, facilitating access for computer programs, maintaining data bases, providing long-term support for collections of monoclonal antibodies and to try to develop new model systems and encourage research using non-mammalian systems and invertebrate systems. Finally a very unusual finding was an idea for how the mass of biological knowledge which they are now calling the "matrix of biological knowledge," how its contribution to our knowledge could be amplified by looking at it in much, much more detail.

Various animals, and systems are studied up the evolutionary scale; various phenomena are common across many of these systems, but the interrelationships and the similarities have really never been fully exploited, and this committee proposed that we take some steps to look at all these data bases of biological knowledge on all the systems and animal species, and try to find the relationships between them.

It is a complicated problem of information handling. Computerization of data bases, linking them together, asking certain questions about certain processes of development or regulation, or chemical transmission, and so on. We have pursued that to some extent already, and hope to continue further.

We have also looked at other kinds of biomaterials that are needed for biological research, and have really only a preliminary grip on that one, but are hoping to define more closely the kinds of resources that scientists need. We will attempt to supply them through this program.

Mr. Conte. Thank you, Doctor.

Thank you, Mr. Chairman.

Mr. Natcher. Mr. Stokes.

MINORITY HIGH SCHOOL STUDENT RESEARCH APPRENTICE PROGRAM

Mr. Stokes. Dr. Pickett, you have mentioned the Minority High School Student Research Apprentice Program which is funded at $1.5 million.

Dr. Pickett. Exactly.

Mr. Stokes. I am very pleased to see that this program did not share in the 1986 Gramm-Rudman reductions.

Dr. Pickett. No, it did not.

Mr. Stokes. Can you tell us why you decided to protect this particular program?

Dr. Pickett. I hate to invoke common sense, but let me do that at this point.

It seemed to me that the 4.3 percent that we were to take away from that program would eliminate 43 high school students from participating in the program. I felt that I should protect those 43 high school students from the likes of me and should not take the cut there.

Well, I don't have to explain to you, sir, the potential that we would perhaps be missing. We absorbed the cut in one of the bigger parts of the BRS Program, in order to protect them.

Mr. Stokes. I just wish we could invoke some of that common sense into some other areas.

Dr. Pickett. Yes, sir.

Mr. Stokes. How many students now participate?

Dr. Pickett. One thousand.

Mr. Stokes. Three hundred institutions?

Dr. Pickett. Two hundred ninety-seven.

Mr. Stokes. Of course, this program is predicated upon the fact that many of these young students will go on to pursue science majors in college?

Dr. PICKETT. That is the idea.

Mr. STOKES. Do we have some data regarding that?

Dr. PICKETT. I will give you some highlights. We looked at the 1984 progress reports that came in from the schools. We find that 96 percent of the students are planning to attend college, and 68 percent of them say they would like to go into biological and health sciences. More than half said doing this in the summer influenced them in thinking about a career in health sciences.

There are more girls than boys in the program.

Most of them are in for at least two or three summers. The program reaches mostly blacks; 56 percent of the students are blacks, 18 percent are Hispanics and so forth.

I have some other details for the record.

[The information follows:]

MINORITY HIGH SCHOOL RESEARCH APPRENTICE PROGRAM SURVEY RESULTS

In a survey conducted in 1984 of students participating in the Minority High School Student Research Apprentice (MHSSA) Program, the following results were reported:

The program is reaching both male (41%) and female (59%) high school students.

It was found that 86% of the students had been in the program for only one summer; 12% for two and 2% for three summers.

The program is reaching different minority groups as shown below: Blacks (56%); Hispanic (18%); Asian (21%); and American Indian (5%).

Students reported the following accomplishments:

Gave a talk at seminar or symposium (36%);

Worked with supervisor on publication (18%);

Received an award such as scholarship or science medal (17%).

Program's influence on student's future plans:

96% of students plan to attend college.

College major planned: Biological and health, sciences (68%); Other majors such as arts, law and engineering (13%); and, Unknown or not indicated (19%);

Program influenced student to pursue research career: yes (85%); no (17%); undecided (25%);

Future career choices of students: Biological and health professional sciences (71%); Other fields (10%); Undecided (19%).

ACCOMPLISHMENTS IN THE RCMI PROGRAM

Mr. STOKES. You have discussed the Research Centers at Minority Institutions Program in response to Mr. Conte's questions. Tell us about some of the accomplishments under that program in 1985?

Dr. PICKETT. It is a little bit early. We don't have a report yet. We will be getting a progress report in about three months after the anniversary date, which is September 30.

However, we have been in touch with them. They are all getting under way and we have seen their advertising for the faculty, and support staff they are trying to recruit. We have seen that in the scientific journals so all I can say is, they are getting under way.

Mr. STOKES. I have seen a great deal of the excitement in these institutions over this program and the opportunities that it represents.

Were 7 RCMI awards made in 1985?

Dr. PICKETT. Yes.

Mr. STOKES. What was the range in priority scores?

Dr. PICKETT. One hundred fifty-three to 189 was the priority score range.

Mr. STOKES. Nine were approved but unfunded applications?

Dr. Pickett. Correct.

Mr. Stokes. Do you believe that these applications are of scientific merit?

Dr. Pickett. Yes, priority scores ranged on a scale from 204 to 389; that is to say, some of them are obviously applications of higher quality than others.

ADMINISTRATIVE SUPPORT FOR RCMI PROGRAM

Mr. Stokes. Doctor, how many staff persons are associated with the RCMI program?

Dr. Pickett. Two, a GS-15 program director and a GS-6, secretary grants technical assistant, plus myself, plus Dr. Raub, because we are both very much involved in the operation of the program. And a grants management staff, of course, is of key importance in getting those applications together and getting them on the road.

Mr. Stokes. Is staffing adequate?

Dr. Pickett. Oh, yes, I think so.

Mr. Stokes. How are the administrative costs associated with the RCMI program—travel, site visits, consultants and so forth—financed?

Dr. Pickett. As far as the site visits, those were funded through the central NIH fund called the General Expense Fund. We did not take those costs out of the $5 million that was available for grant awards.

The travel of the professional staff person is also funded by the General Expense Fund.

Mr. Stokes. Dr. Pickett, I am sure you know a rescission proposal is now pending for the RCMI and the area initiatives. Can you tell us how this proposal came about?

Dr. Pickett. No, sir, the funds are not in DRR's appropriation. They are in the NIH Office of the Director's Appropriation. The rescission did not come through my office. DRR had no rescissions leveled against it.

Mr. Stokes. Are you aware that the National Science Foundation has proposed in its fiscal year 1987 budget a new program, Research Centers of Excellence, at minority institutions—a program which was modeled after the RCMI program?

Dr. Pickett. I am not aware of that. If that is true, immitation is the most sincere flattery. I was not aware of that.

Mr. Stokes. I was very pleased to learn that myself.

Can you highlight some of the research conducted under the Minority Biomedical Research Support Program?

Dr. Pickett. The Minority Biomedical Research Support Program conducts research across the board from the behavioral sciences to chemistry to biochemistry to basic biology. We highlighted a couple of very basic biology studies of an aquatic plant or animal that had some—I would like to do that for the record.

Mr. Stokes. That would be fine.

[The information follows:]

Research Highlights—MBRS Program

Substances isolated from mosslike sea animals called bryozoans possess antibiotic and antitumor properties. Discovered by MBRS-supported researchers at the State University of New York College at Old Westbury, the yet-to-be characterized compounds inhibit the growth of gram-positive bacteria, including those that cause toxic shock syndrome. Assays also show that extracts from two bryozoan species suppress cell division, suggesting that the unknown active agents might check the cellular proliferation that is characteristic of cancer. Scientists are now working to determine the chemical identity of the promising compounds.

At the Univeristy of Texas in San Antonio, a minority scientist supported by the MBRS Program is seeking to identify the genes that are believed to cause the uncontrolled growth of cancer cells. When he fused old cells—those that no longer divide—to young cells, he found that the hybrid cells grew very little. But when malignant cells and old healthy cells were fused, the hybrids behaved like cancer cells, growing uncontrollably.

These findings indicate that certain gene sequences or other factors in cancer cells can reignite the old cells' ability to grow. Using recombinant DNA technology, this MBRS scientist will introduce individual genes from cancer cells into normal cells. With this approach, he hopes to identify the DNA sequence that instructs cancer cells to continue to grow and divide.

Scientists have identified chemicals that may slow the destruction of acetylcholine, the neurotransmitter that is markedly deficient in the brains of patients with Alzheimer disease. In animal studies conducted at the University of Texas in El Paso, MBRS-supported researchers found that certain sulfonyl fluorides significantly inhibited the destructive activity of the enzyme cholinesterase (ChE). The ChE inhibitors appeared to be most active in the brains of animals, having relatively little effect on ChE present in other tissues. Because acetylcholine, the target of ChE, plays an important role in memory, the researchers speculate that treatment with sulfonyl fluorides may improve the memory of Alzheimer patients. The chemicals may help conserve the sparse supplies of acetylcholine synthesized in the patient's brains. Other ChE inhibitors have been evaluated clinically in human patients, but these chemicals also inhibited ChE activity in other organs, where the enzyme plays an important metabolic role. The scientists are continuing basic studies of the sulfonyl fluorides' biological activity in animals. The results may suggest ways to design drugs that are more effective than the original compounds.

An MBRS grantee from the University of Puerto Rico, Rio Piedras has made numerous contributions to research on schistosomiasis. Most recently, he has produced highly defined, species-specific antigens to the parasite. Using monoclonal antibody techniques he is using the antigens to develop improved tools for immunodiagnosis at earlier stages of the disease.

Colchicine is a chemical, produced in plants, which stops cell division when applied to living mammalian cells. Colchicine is known to bind tightly to tubulin, the building blocks of the cell's microtubules. It is postulated that colchicine is mimicking a regulatory chemical which occures naturally in mammals and which may be involved in the control of cell division. In order to study the interaction of colchicine with tubulin, to study the nature of the colchicine binding site, and isolate the regulatory factor, MBRS investigators at the University of Texas, San Antonio have been developing some new research tools. They have synthesized a fluorescent probe, a derivative of colchicine, and have studied its binding to tubulin. This has allowed them to determine that colchicine has multiple binding sites to different portions of the tubulin molecule.

MBRS COFUNDING

Mr. Stokes. Tell us how much was contributed to this program by other Institutes at NIH in 1985 and what are your 1986 and 1987 estimates?

Dr. Pickett. For 1985, the other Institutes at NIH contributed $9,679,000. I should add that NIMH contributed $1,244,000, and the National Institute on Alcoholism and Alcohol Abuse contributed $20,000.

In the 1986 appropriation the other NIH Institutes were scheduled to contribute $9,925,000 and NIMH was $1,171,000, and the Alcohol Institute was the same, $20,000.

The revision of the 1986 budget through sequestration reduced it to $9,497,000 for NIH, and $1,121,000 for NIMH.

The 1987 request is at the level of $9,493,000 from the other NIH institutes.

UNDERGRADUATE AND THEMATIC AWARDS

Mr. STOKES. Last year, we discussed the thematic award, and the four-year undergraduate initiative under the MBRS program. How are these initiatives working and how much is budgeted for them in 1986 and 1987?

Dr. PICKETT. Three awards were made under the thematic initiative in 1985 at a cost of approximately $950,000 with co-funding. We awarded nine undergraduate awards in 1985 at a cost of $962,000.

In 1986, one thematic award was made, and no new undergraduate awards made. We are accepting only undergraduate initiative applications in 1986. We are not accepting any more thematic applications this year.

Mr. STOKES. Please provide for the record a list of the institutions participating in the thematic initiative and also a list of those colleges participating in the undergraduate initiative.

[The information follows:]

MINORITY BIOMEDICAL RESEARCH SUPPORT THEMATIC PROJECT GRANTS—FY 1985

Grant No., Name of Institution, City, State

S11RR02657—University of Puerto Rico, San Juan, Puerto Rico.
S11RR02660—Florida A&M University, Tallahassee, Florida.
S11RR03043—Tuskegee Institute, Tuskegee, Alabama.

MINORITY BIOMEDICAL RESEARCH SUPPORT GRANTS FOR UNDERGRADUATE COLLEGES—FY 1985

Grant No., Name of Institution, City, State

S14RR02639—College of the Virgin Islands, St. Thomas, Virgin Islands.
S14RR02640—Cayey University College, Cayey, Puerto Rico.
S14RR02645—Bennett College, Greensboro, North Carolina.
S14RR02646—Coppin State College, Baltimore, Maryland.
S14RR02649—Shaw University, Raleigh, North Carolina.
S14RR02715—Clark College, Atlanta, Georgia.
S14RR02717—Mississippi Valley State University, Itta Bena, Mississippi.
S14RR02721—St. Mary's University, San Antonio, Texas.
S14RR02866—Rust College, Holly Springs, Mississippi.

Mr. STOKES. Thank you, Mr. Chairman.

GENERAL CLINICAL RESEARCH CENTERS

Mr. EARLY. Doctor, you earlier told the committee that you are reducing the clinical research centers from 78 to 76. Which two are you eliminating?

Dr. PICKETT. We don't know yet. We will look at the competing awards that come up for review this year and those that are on the bottom of the priority list will be the candidates. We know who is up for competition this year, but we don't have all the final reviews and priority scores in and we won't know until after the June Council.

Mr. EARLY. Won't it be determined by how much potential they have? Will it be determined by who are the two lowest?

Dr. PICKETT. Yes, sir.

Mr. EARLY. How much did the cost of conducting clinical research increase in 1985?

Dr. PICKETT. I will provide that information for the record.

Mr. **Early**. Well, provide that for the record and also provide estimates for 1986 and 1987, please.

[The information follows:]

Increased Cost of Conducting Clinical Research

According to the federal government's consumer price index released October 23, 1985, the cost of conducting clinical research and providing medical care increased 6.6 percent during the 12-month period ending September 30, 1985. In formulating the 1986 budget, we assumed the cost of conducting clinical research would increase by 6.2 percent. For 1987, we assumed the cost would increase by 6.0 percent.

Mr. **Early**. How many research beds were supported in 1985?

Dr. **Pickett**. Five hundred ninety-eight.

Mr. **Early**. For the record, supply how many were supported under the original 1986 appropriation, and how many will be supported under the 1986 revised and tell the committee, if you can, how many will be supported under the 1987 budget request?

Dr. **Pickett**. I will do that.

[The information follows:]

Number of Clinical Research Beds 1985-1987

In 1985, the General Clinical Research Centers (GCRC) Program supported 598 clinical research beds. In 1986, at the appropriation level, funds would be available to support approximately 584 clinical research beds and at the 1986 revised level of funding approximately 560 beds would be supported. The 1987 request provides support to fund approximately 528 clinical research beds through the GCRC Program.

CLINICAL ASSOCIATE PHYSICIANS

Mr. **Early**. How many Clinical Associate Physicians were supported in 1985?

Dr. **Pickett**. In 1985, there were 47, and that is what we have right now. The total number supported has been 177 since 1974. One hundred thirty have finished training and 57 have NIH grants, and most of them have stayed in academic medicine.

Mr. **Early**. Expand on that for the record.

[The information follows:]

Clinical Associate Physician Program

In the Clinical Research program, the General Clinical Research Centers (GCRC) provide an ideal facility for clinical research training of medical students, house staff, physicians in postdoctoral positions, and nursing and dietitian students. The Clinical Associate Physician (CAP) Program is a subactivity within the GCRC Program which supports young clinical investigators—physicians who have completed fellowship training—for up to two years, to enable them to begin clinical research careers under the tutelage of senior GCRC investigators. During 1985, the Program funded 47 CAP positions, 13 of which were new positions. Since the CAP Program's inception in 1974, 177 CAP awards have been made; 130 individuals have completed their research training, and so far, 57 of them have been successful in obtaining NIH research support. All but 14 of the former CAPs are in academic positions.

CLINFO MAIL NETWORK

Mr. **Early**. Last year, you indicated that a pilot program was being undertaken to explore the feasibility of designing a nationwide clinical research information and data management system. Has this project been completed?

Dr. **Pickett**. Yes, this is the CLINFO mail network, and we expanded it to linking 40 sites. We are ready now to link all 78 of the centers together, either through their CLINFO or personal computers.

Mr. EARLY. What was your opinion of the results of the trial?

Dr. PICKETT. I think it is going to be very useful for exchanging clinical trial information, common protocols, new techniques and so forth.

Mr. EARLY. Expand on that for the record.

[The information follows:]

CLINFO MAIL NETWORK

Forty General Clinical Research Center (GCRC) CLINFO sites have been linked during the past year through an electronic mailnet and are also linked to the Division of Research Resources. The mailnet allows investigators at General Clinical Research Centers to exchange information, reports and clinical research data.

Administrative Coordinators and System Managers are able to communicate important information or answer questions without the use of telephone or letters. Examples are questions about the progress report, about the use of the CLINFO system, the use of personal computers, and about meetings. The mailnet also allows the exchange of short computer programs between system managers.

The following are examples of telephone calls or correspondence which are being avoided by direct communication via electronic mailnet between GCRCs and DRR. From the GCRCs to the Division, we have received questions about grant awards, about updates of equipment, submission dates for proposals, and questions about patient care costs. From the Division to the GCRCs we have provided notification of delays of grant awards, the need for further information before an award can be made, request for updates on progress reports, receipt of grant reviews done at site visits or mail review, invitation of site visitors and information for GCRC Committee members on upcoming meetings. These mailnet communications have cut down on time spent at the telephone, especially if one of the two parties is out of town or if there is a difference in time zones, and a considerable amount of paperwork and filing.

The CLINFO system has been used to set up multicenter clinical trials. In these preliminary studies, the CLINFO mailnet has been found useful in providing quick and simultaneous display of consent forms for additions and changes, easy communications of changes in the protocol, and a fast and efficient way for communicating any serious side effects occurring during the performance of drug studies.

Mr. EARLY. Have you budgeted money in the 1987 request to do all the things that should be done with that?

Dr. PICKETT. We will be able to operate the CLINFO network and by negotiating awards downward in 1987, we will be able to maintain support to 76 general clinical research centers.

I think we will be able to operate effectively.

BIOTECHNOLOGY RESOURCE CENTERS

Mr. EARLY. I see.

Doctor, the justification indicates that there will be one less biotechnology resource center, from 61 to 60. Have you identified which one will be eliminated?

Dr. PICKETT. No, we have not. We have the same situation as with the clinical centers. Those that are up for competition will be the candidates to look at for elimination, and if we have a renewal with a significantly lower priority score than those above it, that will be the candidate.

PRIMATE CENTER RENOVATIONS

Mr. EARLY. I was interested in your comments to Chairman Natcher with regards to the primate centers. Have we got adequate funds in this budget to continue to update them so we are not subject to being charged with being cruel to animals?

Dr. PICKETT. We made a five-year plan based on a survey of the needs of the centers and we are tracking along on that path.

We have a million dollars budgeted this year. We know the items they want and——

Mr. EARLY. Did the five-year plan call for a million dollars?

Dr. PICKETT. Per year. We wouldn't reach $13 million in five years, but a million dollars a year. We have budgeted a million dollars for this year.

There is one problem that may slow us down, and that is that the new *Guide For the Care and Use of Laboratory Animals* calls for larger cages for certain common sizes of monkeys.

Mr. EARLY. I would think that would be a big expense. Do you have money in your 1987 request for that?

Dr. PICKETT. It will have to be done, and we will have to put priority on that requirement.

Mr. EARLY. How much it will cost?

Dr. PICKETT. Two million dollars is the estimate.

Mr. EARLY. Well then, we are not going to do it all. Supply for the record what we are not going to do, because you don't have the money to do it. We cannot tell people we are going to try to update our facilities with regards to primate centers, and not put the money in to do that.

[The information follows:]

PRIMATE CENTER RENOVATIONS

An extensive assessment of primate center needs was undertaken in 1983 as a result of increasing recognition that center physical facilities and equipment, were seriously deteriorating and becoming out of date. An evaluation panel of outside experts noted the fact that the centers had been constructed in the early 1960s and that repairs, remodeling, and in some cases, expansion of physical facilities were necessary. Similar concerns were expressed about worn out and obsolete equipment, particularly inadequate caging and housing for center animals. These problems made it unlikely that each center could continue to provide optimal care and maintain accreditation by the American Association for the Accreditation of Laboratory Animal Care (AAALAC). They also seriously threatened the center program goal of becoming self-sufficient in breeding the most commonly used species. The results of this assessment showed that accomplishing needed center improvements would cost $13.5 million.

A five year program was begun in 1984 to address these needs with an earmark of $1.0 million included in report language in the 1984 appropriation bill. Additional Federal allocations totalling $2.5 million through FY 1984 and 1985 have made possible a number of improvements. These have included the replacement of leaking roofs, upgrading sewage systems, bringing utility services up to code, providing sources of emergency power, purchasing modern caging, and renovating and reequipping animal facilities and laboratories. The substantial progress made has resulted in six of the seven centers now being accredited by AAALAC, and the expectation that the seventh one will be accredited within the next year. Unforeseen expenses have been added this year to the improvement program. The basic reference document for implementation of the Public Health Service's animal welfare policy, the "Guide for the Care and Use of Laboratory Animals" as revised in 1985, now recommends larger cages for one of the most numerous classes of macaque monkeys. Purchase of these cages and provision of the space that will be necessary to accommodate them will cost approximately $2.0 million. With the incorporation of this change, it is estimated that a total of $12.0 million will be required for completion of the program in addition to the $3.5 million that has already been allocated.

For meeting short term primate center needs, the highest priority for available funds is assigned to physical facility alterations and renovations and equipment purchases that have already been identified. A primary objective is assuring that accredited center programs of animal care remain so and that the single center presently not accredited achieves and maintains that status on the most rapid timetable possible. Successful fulfillment of many of the needs in this program is possible with continued allocations of federal funds. This funding will continue to be supplemented by contributions from host institutions and other sources. To meet additional needs that may occur, such as the current new requirement to provide larger caging, the currently conceived improvement program may have to be extended beyond 1989.

USE OF CHIMPANZEES IN AIDS RESEARCH

Mr. EARLY. Doctor, is the chimpanzee the only animal used on AIDS, on the development of vaccines?

Dr. PICKETT. No, they are not the only animal——

Mr. EARLY. Well, have we protected our supply?

Dr. PICKETT. There are 1,200 chimps available in this country for research.

The supply of chimps may not be adequate down the road. It takes a long time to raise a chimp up to maturity.

Mr. EARLY. If you don't have the money for this year, you have a one-year interruption, might we not have the number we need down the road?

Dr. PICKETT. The budget for the Office of the Assistant Secretary for Health has an item in the AIDS budget which proposes to carry out a plan for chimpanzee research and breeding which would begin with a colony of 250 breeders and attempt to produce 35 offspring per year for the next several years.

Mr. EARLY. There is money in this budget?

Dr. PICKETT. It is in the OASH request.

SUPPLY OF RHESUS MONKEYS

Mr. EARLY. Are you satisfied on the development of the Rhesus monkeys?

Dr. PICKETT. With the supply?

Mr. EARLY. Yes.

Dr. PICKETT. Yes. We had a problem a few years back but we seem to be in quite good shape now.

Several of the centers have ample supplies as of this moment.

DRR BUDGET REDUCTIONS

Mr. EARLY. Doctor, you suggested that we need $2 million for new cages.

Dr. PICKETT. This is discussed in more detail in the primate center report submitted to the committee on the immediate and long-range needs of the centers.

Mr. EARLY. If I go back to my constituents and tell them I am trying to protect the animals in these centers, I want to have the money to do that. Doctor, I was also very impressed with your comments on the shared instrumentation, because everyone wants to get there.

You indicated that the biomedical research support grant program provides flexible funds whose use is determined by the Institutions, and this flexible fund is going to be eliminated. You mentioned to Mr. Natcher alternate sources; you said they would be able to seek additional funds from within the institution or other private sources.

We are making all kinds of cuts, there is not a program in the 1987 request, Doctor, where you are not asking the Institute to take a tremendous reduction.

Is this the biggest reduction in your career there, and you have been associated with NIH almost thirty years.

Is this the biggest reduction you have ever seen?

Dr. PICKETT. The biggest single reduction I have personally seen.

Mr. EARLY. It is hard to say it with all the people around but it is, isn't it?

Dr. PICKETT. Yes, sir.

Mr. EARLY. How can we suggest that they are going to make up this money? Specifically, will you tell us whether the institutions should increase tuitions?

Dr. PICKETT. I think not, sir.

Mr. EARLY. Do you see a big flow of private sources to fund these programs, Dr. Pickett?

Dr. PICKETT. I cannot specify any at this moment, no.

SHARED INSTRUMENTATION

Mr. EARLY. Doctor, DRR is important. It is not the most visible place, but it is so important.

On shared instrumentation, the NMR, are you satisfied that we are going to be able to share those adequately throughout the country?

Dr. PICKETT. Yes, they are the second most popular piece of sophisticated instrumentation that we have provided through this program. It has come up over the past several years, but electron microscopes are still number one.

Yes, I think they will be shared.

Mr. EARLY. One final question, Dr. Pickett.

On shared instrumentation, would you try to link a stabilizing plan with X number of dollars each year. Will your 1987 budget at least keep pace with what you are supposed to do to keep the plan in effect?

Dr. PICKETT. The 1987 budget is pretty close.

Mr. EARLY. Pretty close, it might be a little higher?

Dr. PICKETT. A little bit less than in the 1986 appropriation, and somewhat more than in the 1986 revised.

Mr. EARLY. There is not anything that is less than 1986 revised. How is it compared with 1985?

Dr. PICKETT. Just a shade less in 1985, approximately the same level.

Mr. EARLY. Is the equipment getting cheaper?

Dr. PICKETT. No, sir.

Mr. EARLY. So we are getting a lot less.

Thank you, Mr. Chairman.

Mr. NATCHER. Dr. Pickett, on the record, we want to thank you and your associates for appearing before our committee at this time on behalf of your budget request for the fiscal year 1987.

This has been a good hearing and we appreciate it.

Thank you very much.

The committee will now adjourn until ten o'clock in the morning.

[The following questions were submitted to be answered for the record:]

BIOLOGICAL MODELS AND MATERIALS RESOURCES SECTION

Mr. Conte. What hope does the work of the Biological Models Section hold for reducing the numbers of higher animals used in biomedical research?

Dr. Pickett. The mission of the Biological Models and Materials Resources Section is to develop and support the use of cell systems, lower organisms, and nonbiological systems as models in biomedical research sponsored by NIH, and to provide biological materials and model systems to the research community.

Biological models and materials are used by investigators to solve major problems in biomedical research. Examples of model systems include in vitro cell systems and lower organisms, which are biological materials, and mathematical models or computer simulations which are not biological materials. Biological materials can include some useful research tools such as hormones, c-DNA probes, or human chromosome-specific DNA libraries, which are not, strictly speaking, model systems.

Although higher research animals will always be needed for the conduct of biomedical research, it is hoped that the model systems developed and supported by this section will be able to reduce the numbers of higher animals used in biomedical research.

ANIMAL FACILITIES IMPROVEMENT PROGRAM

Mr. Conte. In 1985, the Division instituted a change in the Animal Facilities Improvement Program to help bring the care and treatment of animals up to acceptable levels. How many applications have you received under this program in FY 1986, and how many will actually get funded?

Dr. Pickett. A total of 100 applications was received in 1985 requesting $38.6 million, including $16.2 million for equipment and $20.8 million for alterations and renovations. The latter category was matched by a $29.5 million institutional commitment. Seventy-four applications were recommended for approval with budgets totaling $20.164 million. Twenty-three one-year awards were made late in fiscal year 1985 totaling $8.571 million. Since we had 51 approved unfunded applications in house, they were carried over and made available for funding in 1986. The FY 1986 budget contains $3.810 million for this program. It is expected that approximately 9 new animal facility improvement projects will be made in 1986.

Mr. Conte. Do you think we are providing enough support to these institutions to correct the problem of inhumane care of animals?

Dr. Pickett. In 1978, the Institute of Laboratory Animal Resources of the National Research Council conducted a survey which provides the only available detailed data upon which to base estimates of the scope of the problem and represents a reasonable assessment of present needs. The survey findings are summarized below.

1. About 16% of all nonprofit biomedical research organizations reported a need for replacement of some animal facility space now in use, 38% reported a need for remodeling to protect the integrity of space now in use, and 43% reported a current need for additional space.

2. The 1978 needs of nonprofit biomedical research organizations for space replacement, remodeling and additions to their animal facilities would have required $350 million. Another $407 million would have been needed to meet space needs projected from 1978 through 1988. These same organizations reported a need in their replacement or additions.

A survey in 1979, conducted by the National Cancer Institute, was directed to extramural cancer research institutions. Total current (1979) construction needs were $221 million; of this, $34 million or 15% was for animal facilities. The long range (five year) total requirement was $449 million, of which $51 million or 11% was for animal facilities.

In addition, the applications submitted in response to the Animal Facilities Improvement Program indicate the extent of unmet need in at least 74 research institutions for improvements to their animal facilities. These 74 approved but unfunded applications requested more than $28 million from DRR and indicated that they had access to matching funds from other sources.

IMPROVEMENT IN THE CARE OF RESEARCH ANIMALS

Mr. Conte. Doctor, are we seeing good improvement in the care of research animals, and what other mechanisms, besides grant money, does the Division use to help institutions correct problems they may have?

Dr. Pickett. We are seeing much improvement in the care of research animals. The Office of Protection from Research Risks (OPRR) at NIH has revised the PHS Animal Welfare Policy and developed a number of strict requirements in this new policy. The principal changes are:

1. More specific identification of responsible officials and administrative structure for the institutional animal care program.

2. A veterinarian experienced in laboratory animal medicine must supervise the animal health care program and be a member of the institutional animal care program.

3. The institutional animal care committee must have a member who is not a scientist and one who is not a member of or related to a member of the research institution's staff. These needs may be met by one and the same person.

4. Institutions must report on their organizational structure, management system, procedures used and both the size of their facilities and the size of their animal population.

5. The Animal Care Committee must review and approve research protocols using animals that are part of any PHS application.

6. All research institutions (grantees) must be American Association for the Accreditation of Laboratory Animal Care (AAALAC)- or self-accredited using the NIH Guide for the Care and Use of Laboratory Animals. Deficiencies must be reported together with a plan to correct them.

7. The OPRR may decide to make site visits to any grantee institution to evaluate the animal care program. Formerly, AAALAC-accredited institutions were exempt from these visits.

8. The new policy provides for waiver of a policy provision or provisions.

RESEARCH INSTRUMENTATION NEEDS

Mr. Conte. The justifications say that your budget request to the committee "recognizes the importance of stabilizing" support for research instrumentation. On the other hand, this report we just got on the fifty-second meeting of the Director's Advisory Committee says that problems are "widespread", and the needs out there are great, especially for the smaller instruments. Your budget proposes to cut out the Biomedical Research Support Grants, so what's left? Isn't the problem going to get worse, not better as the justifications would imply?

Dr. Pickett. The 1987 budget request for the Biomedical Research Support Program is $32,883,000, of which $31,383,000 is for support of the Shared Instrumentation Grant Program. These funds will enable the Program to continue to make available large, expensive instrumentation -- in the $100,000 to $300,000 cost range -- to institutions for groups of PHS-funded investigators on a shared-use basis. The remaining $1,500,000 is for the Minority High School Student Research Apprentice Program.

FUNDING FOR THE SIG PROGRAM

Mr. Conte. Doctor, we've discussed in the past the study NIH did a few years ago on shortages in research equipment and instrumentation. The recommendations of that study were that over a five year period, ending in FY 1987, the Shared Instrumentation Grants (SIG) Program should get annual $5 million dollar increases. Has this program received those annual increases each year since FY 1983?

Dr. Pickett. The Shared Instrumentation Grant Program received increases of at least $5 million per year in 1983, 1984, and 1985. Under the 1986 revised level, the Program has been reduced by $1.2 million. The 1987 budget request provides an increase of $1.0 million over the 1986 revised level.

Mr. Conte. The request for FY 1987 shows a slight increase over 1986 for this program, but still an overall decrease from the 1986 appropriations level. What effect will this small increase have on the program? Will you be able to make more awards?

Dr. Pickett. The 1987 request for the SIG Program is $31,383,000, an increase of $1,009,000 over the comparable 1986 revised level of $30,374,000. The Division expects to make approximately 154 SIG awards in 1987, 2 fewer than the number estimated in 1986, owing to the increased costs of purchasing high technology instrumentation.

RESEARCH TRAINING

Mr. Conte. Doctor, your request also proposes to eliminate all funds for new training positions in FY 1987. Was this decision made downtown or out at Bethesda?

Dr. Pickett. The decision regarding numbers of research training positions was made at the NIH level.

Mr. Conte. What kinds of researchers does the Division train?

Dr. Pickett. The Division of Research Resources trains laboratory animal veterinarians to provide professional care of the many species of laboratory animals, to manage central animal resources, and to give special assistance to investigators through knowledge of laboratory animal biology and understanding of research methods. In addition, the trainees are prepared to participate in the teaching of graduate students and young investigators and to pursue their own research interests either as independent investigators or as members of a research team.

In addition, the Division provides training opportunities through several non-National Research Service Award Act mechanisms. The Clinical Associate Physician (CAP) Program, supports young clinical investigators -- physicians who have completed fellowship training -- for up to two years, to enable them to begin clinical research careers under the tutelage of senior clinical investigators. The Minority Biomedical Research Support (MBRS) Program helps to increase minority representation in biomedical research by promoting minority faculty and student participation in all areas of biomedical research at eligible MBRS institutions. Within the Biomedical Research Technology (BRT) Program, training in the use of instruments, new technologies, and research methodologies are an integral part of BRT center awards.

Mr. Conte. Do you fully support this proposal to eliminate all new training positions, Doctor?

Dr. Pickett. It is expected that the levels contained in the budget will ensure a reliable continuum of creative, qualified scientists entering research careers.

PRIMATE RESEARCH CENTERS

Mr. Conte. Just a couple of years ago this committee began an aggressive 5-year modernization program for the Regional Primate Research Centers. Will that plan continue under the budget request?

Dr. Pickett. Yes, it will. The 1987 budget request includes $1,000,000 to continue to address the repair and renovation needs of the Primate Center. These funds will be used for major roof repairs at several centers, to improve sewage disposal systems, renovate ventilation and sanitation equipment, provide additional caging and cage washing equipment, and replace obsolescent central research equipment.

Mr. Conte. How many of the seven centers are now accredited?

Dr. Pickett. Six of the seven primate research centers are currently accredited by the American Association for the Accreditation of Laboratory Animal Care (AAALAC).

Mr. Conte. When do you expect they'll all be in line?

Dr. Pickett. The Primate Research Center at the University of Wisconsin has not yet been accredited. The University of Wisconsin has advised DRR that it will apply for accreditation by the American Association for the Accreditation of Laboratory Animal Care by September 1, 1986. By that time, a modernization and improvement program that is presently underway in the College of Letters and Science, of which the Primate Center is a component, will have proceeded to the point where AAALAC is expected to grant accreditation at least on a provisional basis.

HTLV III-LIKE VIRUS IN MONKEYS

Mr. Conte. One of the more famous of those Centers is the one up in New England, where they've been doing a lot of work on AIDS. What is the significance of the discovery of an HTLV III-like virus in monkeys?

Dr. Pickett. The success of research that will lead to a human AIDS vaccine will depend greatly on the availability of well characterized animal models for AIDS. Nonhuman primate models for AIDS have been identified in the Primate Centers that are very similar to the disease in man. One of the retrovirus agents that has been isolated from monkeys at the New England Regional Primate Center, known as simian T-cell lymphotropic virus (STLV III), is closely related to the HTLV III that is the cause of human AIDS. Infections with STLV III produce decreased levels of T-4 lymphocytes, T-4:T-8 reversals, opportunistic infections, encephalitis, wasting, diarrhea, immune deficiences and high mortality in experimentally-inoculated animals. Both inactivated HTLV III-like and Immuno-Stimulatory Complex (ISCOM) vaccines produce antibodies when inoculated into rhesus monkeys. Challenge studies are proposed that will show whether or not these vaccines are actually protective.

Mr. Conte. Will that be the logical test site of any potential human vaccines?

Dr. Pickett. Yes, this is one of the Centers where initial vaccine testing in primates is under way and could be expanded.

THE OCTOPUS AS A RESEARCH ANIMAL

Mr. Conte. Just one final question, Doctor. Last year I noted that you provided for the establishment and expansion of colonies of squid. This year I noticed you talk some about the Octopus. What special characteristics does the Octopus have that makes it a good research animal?

Dr. Pickett. The octopus is a member of the cephalopod family. Because cephalopods are the only invertebrates with a closed circulatory system and a highly vascularized brain, they are particularly suitable for studies of the correlations between behavior and the nervous system. Octopuses are important in learning experiments, as they have short- and long-term memory stores. Their vertebrate-like eyes have also been used for studies of phototransduction, corneal regeneration and neural pathways.

Mr. Conte. What other colonies of animals do you support that might seem strange to the lay person?

Dr. Pickett. The Division of Research Resources supports several animal colonies. These include a resource for marine invertebrate models of neurological and other biological processes; and colonies of mutant mice that model endocrine, neurological, and immunological problems.

Another colony recently developed is the short-tailed opossum, a marsupial native to Brazil. This animal has many characteristics that make it ideal for research - small size, tameness, prolific breeding in captivity, and short gestation time. These features are in marked contrast to the severe research limitations of the Virginia opossum, the North American species that is more widely available. The colony project aims to establish a suitable diet and husbandry techniques that will increase production of the short-tailed opossum. Infant opossums and other newborn marsupials are particularly good candidates for immunologic studies because they lack the natural defenses of thymic lymphoid tissue, peripheral blood lymphocytes, and immunoglobulins.

ESTABLISHMENT OF GOALS FOR SENIOR ADMINISTRATORS

Mr. Stokes. Do you establish goals for your senior administrators for addressing minority program and personnel issues? If not, why not?

Dr. Pickett. Yes, we do establish goals for all of our senior administrators for addressing minority program and personnel issues. Performance plans for each Senior Executive Service, each Senior Level Professional and each Senior Level Administrative employee include at least one performance element that ensures that each manager applies affirmative action and equal employment opportunity principles.

Mr. Stokes. How do you hold your senior officers accountable for meeting these goals?

Dr. Pickett. At least three times each year senior administrators and managers meet with their respective supervisors to review their performance, and discuss ways to improve performance. Since each performance plan includes goals for addressing minority program and/or personnel issues, this becomes an important part of each review. All managers are rated on how effectively they apply affirmative action and equal employment opportunity principles. If their performance is lacking in this area, their overall rating reflects this inadequacy, and they are directed to improve their efforts in the future. If performance is satisfactory, managers are encouraged to continue and expand their efforts in this area.

NUMBERS OF BLACKS IN ADMINISTRATIVE POSITIONS

Mr. Stokes. For the record, please supply the following information for SES, Senior Level Professional and Senior Level Administrative positions in your division: the current number of all such positions and the current number of these positions occupied by blacks.

Dr. Pickett. The information is shown in the table below.

	Total Number of Positions	Number of Positions Occupied by Blacks
Senior Executive Service	2	0
Senior Level Professional	12	3
Senior Level Administrative	8	1
Total	22	4

EFFECT OF REDUCTIONS ON GCRCs

Mr. Early. The budget request also proposes to reduce direct costs by 8% in FY 1986 and by 10% in FY 1987. What effect will these reductions have on the size and scope of general clinical research centers? On the research programs at these centers?

Dr. Pickett. General clinical research centers will be negotiated downward by an average of approximately 10 percent from recommended levels in 1987 and 8 percent in 1986, compared with one percent in 1984 and one percent in 1985 resulting from prudent grants management practices. Through careful negotiation of each center's budget we hope to minimize the impact of these reductions. However, without other sources of funding there will be reductions in the number of research beds available for clinical research of approximately 40 beds in 1986 and 70 beds in 1987. The number of skilled clinicians, research nurses, dietitians, and laboratory technicians will also be reduced.

Mr. Early. Given this anticipated increase in the cost of conducting clinical research and the proposed reductions in direct costs, how much of its increased costs will each center be expected to absorb in FY 1986 and FY 1987?

Dr. Pickett. The anticipated increase in the cost of conducting clinical research is 6.2 percent in 1986 and 6.0 percent in 1987. The budget recognizes full council recommended levels for these centers, including these increased costs of conducting clinical research, but requires downward negotiations of approximately 10 percent. As a result, the centers will be expected to absorb all of these cost increases within their awarded grant budgets.

AVERAGE BIOMEDICAL RESEARCH TECHNOLOGY AWARD

Mr. Early. What was the average grant award for a biomedical research technology center in FY 1985?

Dr. Pickett. The average cost of a biomedical research technology (BRT) center in 1985 was $573,000.

Mr. Early. What is your projection for FY 1986 and FY 1987?

Dr. Pickett. The average projected cost is $559,000 in 1986 and $565,000 in 1987.

DOWNWARD NEGOTIATIONS OF BRT CENTERS

Mr. Early. Doctor, the budget justification indicates that there will also be downward negotiations in direct costs for these centers -- 7-8% in FY 1986 and 10% in FY 1987. How do cuts like these affect these centers -- what elements are most impacted?

Dr. Pickett. Reductions in Biomedical Research Technology (BRT) centers will be achieved in 1987 by carefully negotiating the direct cost of each center. The comparable reductions were one percent in 1984 and one percent in 1985 resulting from prudent grants management practices. DRR program staff and grants management staff will carefully examine each center's approved budget request and progress reports, and implement reductions in numbers of personnel, numbers of protocols, supplies, and equipment from approved levels.

Mr. Early. What effect will these cuts have on the programs at these centers?

Dr. Pickett. Although such reductions may delay the completion of some projects and the acquisition and dissemination of scientific knowledge, the Division will be able to continue ongoing efforts at most of the BRT centers.

EFFECT OF REDUCTION ON BRT'S PROGRAM PLANS

Mr. Early. Doctor, will you summarize with some specificity, the effect proposed reduction will have on DRR's program plans -- both immediate and long-range?

Dr. Pickett. In the immediate short-term the 1987 proposed budget reductions may delay the completion of some research projects and the acquisition and dissemination of scientific knowledge resulting from research carried out using the shared resources provided by the Biomedical Research Technology (BRT) program. As a result of the proposed downward negotiations of direct costs at each center, scientists wishing to use the resources may find limited hours of operation; fewer core staff members trained in the appropriate research methods; limits and restrictions placed on users of the centers; and higher user charges imposed upon researchers in order to recoup some portion of the direct cost reductions. Although such reductions may delay research efforts, the Division will be able to maintain ongoing research efforts, for the short-term, at most of the BRT centers.

Over the long-range, the proposed reduction in 1987 will more significantly impact DRR's plans for the Biomedical Research Technology program. Research accomplishments and new scientific advances made in biomedical research technology centers have helped the United States research community to remain competitive in biomedical research technologies, particularly in the development of research and diagnostic instruments in the field of magnetic resonance imaging. The competitive edge may be lost to other countries if U.S. researchers do not have continued access to state-of-the-art technologies and research methodologies. Training of researchers in the use of these sophisticated research technologies is another area in which the Division must concentrate its long range plans.

U.S. COMPETITIVE POSITION IN ADVANCED INSTRUMENTATION

Mr. Early. To what extent have we made any progress in improving our competitive position vis-a-vis Europe and Japan in the area of advanced instrumentation?

Dr. Pickett. In relation to research technologies for biomedical research where significant markets exist, U.S. industry continues to compete effectively in instrument development. For example, U.S. companies are leading the world in the development of research and diagnostic instruments in the new field of magnetic resonance imaging. The U.S. position is less satisfactory in areas, such as electron microscopy and mass spectroscopy, with more limited instrument sales but important potential research applications in biomedical science. Companies from Europe and Japan continue to dominate the advanced instrument markets in these areas.

TRAINING OPPORTUNITIES IN BRT RESOURCES

Mr. Early. Doctor, back in 1984, Congress provided a limited amount of funds to initiate a program to increase training opportunities in biotechnology resources. Bring us up to date on the progress that has been made in this area. How has this initiative worked out?

Dr. Pickett. The 1984 funds were used to augment training activities at existing biomedical research technology resources. Eighteen applicants responded to an announcement of the availability of up to $20,000 per year for training activities to be proposed by the applicants; eleven of the supplementary applications were funded. The program expanded the concept of training both users and students of advanced technology to include activities like use of videotape instruction films prior to traveling to a distant Resource to use a particular instrument or technology, and intensive "hands on" workshops on background needed to use advanced technologies and to design appropriate experiments. Training is an integral part of applications for biomedical research technology resources, and support for the training programs is being integrated into the normal application process.

Mr. Early. What resources have been allocated for this program in FY 86 and FY 87 and how many awards do you expect to make in each year?

Dr. Pickett. We have commitments to maintain supplemental support, amounting to $60,000, to continue to fund training opportunities at 3 resource centers in 1986. In 1987, we expect to maintain supplemental training support to one resource center at a cost of $20,000. No new activities are planned for training opportunities at biomedical research technology centers.

Mr. Early. Last year, we discussed the need to train more scientists in the area of application and technology transfer. One area you identified in which scientists could benefit from increased training was in the design of special purpose, large scale integrated electronic circuits. Are there any initiatives underway in this area?

Dr. Pickett. We still believe that increased training in the design of special purpose, large scale integrated electronic circuits could yield important benefits.

Mr. Early. Do you plan any initiatives in this area?

Dr. Pickett. We do not plan to initiate any new activities in this area at the present time.

COORDINATION WITH THE NATIONAL SCIENCE FOUNDATION

Mr. Early. To what extent do you coordinate activities in this area with the National Science Foundation?

Dr. Pickett. Several Biomedical Research Technology applicants have made use of the National Science Foundation (NSF) sponsored center for custom preparation of integrated circuits. The major support for very large scale integrated circuit design innovation has been from Defense Advance Research Projects Agency (DARPA) which supports the fabrication of circuits through the University of Southern California. Using this service, universities can design very large scale integrated circuits using a standard format, transmit these designs over computer networks and receive finished parts, in small quantitities at a moderate cost.

The NSF has come to an agreement with DARPA through which access to the University of Southern California service is provided for certain NSF grantees and for student projects. One of our resources at Washington University makes significant use of this agreement. Courses are presented and experience with working designs is obtained. The skills developed through this DOD/NSF/NIH cooperation help both industry and the NIH supported biomedical activities at Washington University.

PRIMATE RESEARCH CENTER NEEDS

Mr. Early. Doctor, would you briefly summarize the findings of DRR's report on the immediate and long-range financial needs of the regional primate research centers?

Dr. Pickett. An extensive assessment of primate center needs was undertaken in 1983 as a result of increasing recognition that center physical facilities and equipment were seriously deteriorating and becoming out of date. An evaluation panel of outside experts noted the fact that the centers had been constructed in the early 1960s and that repairs, remodeling, and in some cases, expansion of physical facilities were necessary. Similar concerns were expressed about worn out and obsolete equipment, particularly inadequate caging and housing for center animals. The results of this assessment showed that accomplishing needed center improvements would cost $13.5 million.

A five year program was begun in 1984 to address these needs with an earmark of $1.0 million included in report language in the 1984 appropriation bill. Additional Federal allocations totalling $2.5 million through FY 1984 and 1985 have made possible a number of improvements. These have included the replacement of leaking roofs, upgrading sewage systems, bringing utility services up to code, providing sources of emergency power, purchasing modern caging, and renovating and re-equipping animal facilities and laboratories. The basic reference document for implementation of the Public Health Service's animal welfare policy, the "Guide for the Care and Use of Laboratory Animals" as revised in 1985, now recommends larger cages for one of the most numerous classes of macaque monkeys. Purchase of these cages and provision of the space that will be necessary to accommodate them will cost approximately $2.0 million. With the incorporation of this change, it is estimated that a total of $12.0

million will be required for completion of the program in addition to the $3.5 million that has already been allocated.

Principal long term center objectives include assuring that: 1) programs of exemplary animal care are maintained, 2) there is improved accommodation to the needs of outside investigators, 3) continuing progress is made towards becoming self sufficient in producing those species needed in center programs that can be bred domestically, and 4) cooperative programs with institutions in source countries are strengthened to provide access to those species that cannot be bred in sufficient numbers domestically.

Overall, the most pressing long term need is for space for additional animal holding and for breeding. Specifically, additional facilities of appropriate design are needed for 1) studies that require isolation, such as the development and testing of candidate vaccines against human AIDS, and 2) better separation and protection of valuable breeding colonies that cannot be replaced. An associated requirement is for additional space and equipment for laboratory services and studies, particularly in the areas of microbiology and immunology.

The cost of meeting these currently identified long term needs is estimated at a total of $5 million for equipment purchases and alteration or renovation of physical facilities and $5 million for construction during the next five year period above and beyond the current modernization and improvement program.

More extensive involvement by the Primate Centers is needed in establishing conservation and resource management programs in those countries that still must be relied upon for supply of certain species of nonhuman primates needed in biomedical research and testing programs.

For meeting short term primate center needs, the highest priority for available funds is assigned to physical facility alterations and renovations and equipment purchases that have already been identified.

For meeting longer term center needs, DRR anticipates that funding will continue on a level basis. Some tradeoffs may be required to provide the resources necessary to support expanded breeding and animal holding programs and the needs of outside scientists. Level funding will be sufficient to provide adequate core operational support and the continuing improvement program. Matching funding from host institutions or other sources would be required for any center construction project to be supported with federal funds.

Mr. Early. And would you tell us, doctor, how your FY 1987 budget request addresses these needs?

Dr. Pickett. The 1987 budget request includes $1.0 million to continue to address the immedicate repair and renovation needs of the Primate Centers. These funds will be used for major roof repairs at several centers, to improve sewage disposal systems, renovate ventilation and sanitation equipment, provide additional caging and cage washing equipment, and replace obsolescent central research equipment.

Mr. Early. Do you think we should be moving more rapidly to address these needs and problems?

Dr. Pickett. Successful fulfillment of many of the needs in this program is possible with continued allocations of federal funds. This funding will continue to be supplemented by contributions from host institutions and other sources. To meet additional needs that may occur, such as the current new requirement to provide larger caging, the proposed improvement program may have to be extended beyond 1989.

DRR plans to continue to encourage the development of sources of center funding other than the base operating grant. The development of cost recovery systems offers a good example of how other sponsors, primarily the categorical institutes of NIH, will increasingly help to support the costs of center operations. The cultivation of mutually beneficial relationships between the centers and organizations in the industrial sector also will continue. These approaches will broaden the base of sponsorship for research using center resources and will allow greater flexibility for program funding to meet critical center needs.

Mr. Early. Doctor, how much did DRR request of NIH for primate center repair and renovation in FY 1987?

Dr. Pickett. DRR requested $12.0 million in its 1987 preliminary budget submission to NIH to complete necessary repairs and renovations at the primate research centers.

Mr. Early. And what was the NIH request to the Public Health Service?

Dr. Pickett. The NIH request to the Public Health Service included $1.0 million to continue to address the repair and renovation needs of the primate centers.

IMPACT OF REDUCTIONS ON THE PRIMATE CENTERS

Mr. Early. Given this situation (of need), what impact will the 8-10% direct cost cuts proposed for FY 1986 and FY 1987 have on the primate centers' operational ability and their ability to address these needs?

Dr. Pickett. Reductions of 8 to 10 percent in the primate research centers will be achieved by carefully negotiating the direct cost of each center. DRR program staff and grants management staff will carefully examine each center's approved budget request and progress reports, and implement reductions in numbers of personnel, numbers of research protocols, supplies, and equipment from approved levels. Although such reductions may delay the completion of some projects and the acquisition and dissemination of scientific knowledge, the Division will be able to continue ongoing efforts at most of the primate research centers. In addition, this may reduce the number of nonhuman primates that would normally be available for the use of investigators on institute-supported research project grants.

RESEARCH TRAINING FOR VETERINARIANS

Mr. Early. Doctor, in reviewing your budget request, I see that you are not planning any new research training awards in either FY 1986 or FY 1987. Why is that, since I understand that there continues to be a shortage of well trained laboratory animal veterinarians?

Dr. Pickett. While there continues to be a shortage of well trained laboratory animal veterinarians to direct institutional programs of animal care and use, the problem is not deemed sufficiently critical to warrant funding above the level available in the FY 1987 President's Budget.

ANIMAL FACILITIES IMPROVEMENT PROGRAM

Mr. Early. How has the extramural animal facilities improvement program been working? What has been the response to this initiative?

Dr. Pickett. The extramural animal facilities improvement program has been very well received by the biomedical research community. An announcement was made in the December 7, 1984 NIH Guide for Grants and Contracts describing the program. Institutions were allowed to request up to $500,000 for alterations and renovations (A&R) on a 50:50 matching basis plus needed equipment. A total of 100 applications were received in 1985 requesting $38.6 million, including $16.2 million for equipment and $20.8 million for alterations and renovations. Seventy-four applications were recommended for approval with budgets totaling $20.164 million. Twenty-three one-year awards were made late in the fiscal year totaling $8.571 million.

Mr. Early. How much will be available for this program in FY 1986?

Dr. Pickett. The 1986 revised level includes $3,810,000 for animal facilities improvement awards.

Mr. Early. How much in FY 1987?

Dr. Pickett. The 1987 request includes $3,981,000 for animal facilities improvement awards.

Mr. Early. How many applications do you expect to receive in FY 1986 and how many awards will you be able to make?

Dr. Pickett. The animal facilities improvement program was a new initiative in fiscal year 1985 for which an announcement was made in the December 7, 1984 NIH Guide for Grants and Contracts. A total of 100 applications were received in response to that announcement, of which 74 were recommended for approval. Twenty-three awards were made in 1985 leaving 51 approved unfunded applications. As such, we have chosen not to readvertise the program in 1986. We expect to make approximately 9 animal facility improvement awards in 1986 from among the remaining approved unfunded applications.

Mr. Early. Doctor, how much did DRR request of NIH for this program in FY 1987?

Dr. Pickett. DRR requested $20.0 million of NIH in its 1987 preliminary budget submission for the Animal Facilities Improvement Program.

Mr. Early. And, what was the NIH request to PHS?

Dr. Pickett. Since there were no dollars included in the 1986 President's budget request for an animal facilities improvement program, NIH requested zero dollars in its 1987 budget request to the Public Health Service. Once action was completed on the 1986 appropriation bill, which provided funds for the animal facilities improvement program, the Department of Health and Human Services included $3,981,000 in its request to OMB. This is the amount that is presently included in the 1987 President's Budget.

TERMINATION OF THE BRSG PROGRAM

Mr. Early. Since evaluations of the BRSG program have been favorable, what is the rationale for termination of this program? Was this decision based solely on fiscal considerations?

Dr. Pickett. The Biomedical Research Support Grant Program, which provides generalized institutional support, must rank as a lower priority when compared to other NIH programs which permit the focusing of research funds to specific priority areas. In order to provide continued support to research investigators at those institutions most heavily engaged in biomedical research, institutions will be encouraged to require more sharing of resources and facilities, allow more release time for investigators to conduct pilot research activities, initiate institutional development programs for new investigators, and seek additional funds from within the institution and other private sources.

BRSG FUNDING FOR INSTRUMENTATION

Mr. Early. NIH recently submitted to the Committee a report on its December Advisory Committee meeting which addressed the problem of obsolete biomedical research instrumentation. One of the greatest areas of need for support appears to be for small instruments ($5,000-$60,000 cost). I understand that providing sophisticated equipment to investigators, at times, cannot be justified by any single project. It would seem that BRSG funds are one of the few resources available which would permit institutions to provide such instrumentation for a group of its researchers. Can institutions use their BRSG funds this way?

Dr. Pickett. Yes they can. Institutions may carry forward Biomedical Research Support Grant (BRSG) funds from one year to the next, a provision that permits research centers to plan the purchase of expensive equipment without interrupting funding of smaller projects. BRSG support of central resources and equipment usually requires a collaborative effort among several investigators and departments who will benefit from the purchase. Grantees may also choose to expend their entire BRSG award in a given year on a single in-trument if such an investment is given priority.

Mr. Early. To what extent do institutions use these funds for instrumentation?

Dr. Pickett. Approximately 5 percent of BRSG activities are for the purpose of funding a central facility or shared instrument.

NIH SUPPORT FOR PILOT RESEARCH

Mr. Early. What sources of funds, other than BRSG, are available through NIH to support pilot research to explore new ideas?

Dr. Pickett. While the Biomedical Research Support Grant is unique in the way it provides support for pilot research, the NIH does support several other grant mechanisms that can provide pilot research support to test the validity of new ideas and the feasibility of methods to be employed in the research. For example, the small grant mechanism provides research support specifically limited in time and amount for studies in categorical program areas. Small grants provide flexibility for initiating studies, which are generally for preliminary short-term projects and are non-renewable. Phase I small business innovation research grants support projects, limited in time and amount, to establish the technical merit and feasibility of R&D ideas which may ultimately lead to a commercial product or service.

BRSG FUNDING REQUEST

Mr. Early. How much did DRR request of NIH for this program in FY 1987?

Dr. Pickett. DRR requested $68,476,000 for the Biomedical Research Support Grant program in its 1987 preliminary budget submission to NIH.

Mr. Early. And, what was included in the NIH request to PHS for the BRSG program?

Dr. Pickett. The NIH request to the Public Health Service for the BRSG program was also $68,476,000.

NEW INITIATIVES IN 1987

Mr. Early. Will this budget request enable DRR to undertake any new initiatives?

Dr. Pickett. No, DRR will not be able to undertake any new initiatives in 1987.

1987 FUNDING PRIORITIES

Mr. Early. If an increase over the FY 1987 request is provided, how would you use these additional funds? What would your priorities be?

Dr. Pickett. If an increase to our 1987 budget request was provided by the Congress, our first priority would be to restore full direct cost funding to all of our ongoing awards. Our next priority would be to restore the Biomedical Research Support Grant Program, two general clinical research centers, and one biomedical research technology center, all of which had been planned for elimination under the 1987 budget request. Next, we would expand the animal facilities improvement program in an effort to provide assistance to more institutions. Then, we would propose to support new biomedical research technology centers in the areas of supercomputers, in vivo nuclear magnetic spectroscopy, and new imaging methodologies; support a few new general clinical research centers; and expand support in the MBRS program for thematic project grants and the undergraduate college program. Finally, we would provide additional funds to meet more of the demand for primate center repair and renovation needs.

NEW RESEARCH OPPORTUNITIES

Mr. Early. Will any significant new research initiatives or opportunities be lost or delayed by lack of funds in the FY 1987 budget?

Dr. Pickett. Yes, several new research initiatives will be delayed by lack of funds in the 1987 budget.

Mr. Early. Please provide, for the record, a list of these along with brief descriptions and the funding requirements associated with each.

Dr. Pickett. A list of the new research initiatives that will be lost or delayed follows.

- Within the Biomedical Research Technology Program, there is a need for new resource centers in the areas of supercomputers, in vivo Nuclear Magnetic Resonance spectroscopy, and new imaging methodologies which would serve both basic and clinical research scientists, and would greatly facilitate the creative application of these powerful new tools to biomedical research problems. Initiation of such new centers will require approximately $6.0 million.

- Each of the Primate Research Centers has repair and renovation needs critical to upgrading their animal facilities so that they meet and maintain standards for accreditation set by the American Association for Accreditation of Laboratory Animal Care. Under the 1987 budget request, capacity for completion of repairs and renovations to the Primate Centers will be delayed indefinitely. Approximately $11.0 million will be required to complete the necessary repairs and renovations at the primate centers.

- Improvements to laboratory animal facilities at institutions throughout the country that use laboratory animals in their research will be delayed. Approximately $16.0 million will be necessary to get us started on needed animal facility improvement projects.

- The two Minority Biomedical Research Support initiatives newly launched in 1985, the Thematic Project Grant and the Undergraduate College Award can not be further developed under the terms of the 1987 President's Budget. Approximately $3.0 million will be necessary to provide the needed support to minority institutions for these new initiatives.

- Expanded numbers of research beds within the General Clinical Research Centers Program will not be available to meet the demand for clinical research studies in areas of public health emergencies. Approximately $800,000 will be necessary in order to provide an appropriate number of research beds to conduct these clinical studies.

- Efforts to increase capabilities for diagnostic retrovirology (e.g., isolation, propagation, and identification) and serology studies at the primate research centers need to be undertaken in order to maximize the opportunity these animal resources offer for AIDS research. Further, immunodeficiency disease in the centers poses problems to colony health that should be dealt with by provision of adequate isolation caging and facilities in order to properly contain infected animals and to protect healthy animals and humans at the centers. Approximately $500,000 will be necessary if these initiatives are to be undertaken in 1987.

DELAYS IN ONGOING RESEARCH INITIATIVES

Mr. Early. Doctor, will any significant research initiatives currently underway be halted or seriously delayed due to FY 1987 funding levels?

Dr. Pickett. Yes, some ongoing research initiatives will be affected under the 1987 budget request.

Mr. Early. To what extent will there be major reductions in the scope of ongoing or new initiatives because of the FY 1987 funding levels?

Dr. Pickett. The major impact of the budget is to eliminate support for the Biomedical Research Support Grant Program in 1987. In addition, two general clinical research centers and one biomedical research technology center will also be eliminated. All of the Division's ongoing awards will be negotiated downward by an average of approximately 10 percent below recommended levels. No new initiatives will be started under the funding levels provided in the 1987 budget request.

Mr. Early. For the record, please provide a list of these along with a brief description and the amounts associated with each initiative.

Dr. Pickett. The following is a list of ongoing research initiatives which will be halted or seriously delayed under the 1987 budget request.

- Support for two of the 78 existing general clinical research centers will be eliminated in 1987. The determination as to which 2 centers will be eliminated will be made in 1987 after peer review and the annual ranking process have been completed, which will determine the relative scientific merit of each competing renewal application. It will cost approximately $2.5 million to restore these 2 centers.

- Each of the 76 remaining general clinical research centers will be negotiated downward by an average of approximately 10 percent from recommended levels. This will reduce the number of research beds available for clinical research by approximately 60 which will result in higher overall costs to clinical research investigators. The number of skilled clinicians, research nurses, dietitians, and laboratory technicians will also be reduced. Thus, since the centers enable research on a broad range of disease areas, research efforts in the areas of diabetes, nutrition, hypertension, alzheimer's disease, arthritis, genetics, clinical trials, immunology, prevention, and sexually transmitted diseases, among others, will be reduced and/or delayed as a direct result of a 10 percent average reduction in the level of resource support at the GCRCs. It will cost approximately $9.5 million to restore these centers to full funding.

- Support for one of the 61 existing biomedical research technology centers will be eliminated in 1987. The determination as to which center will be eliminated will be made in 1987 after the peer review process has been completed, which will determine the relative scientific merit of each competing renewal application. It will cost approximately $600,000 to restore funding for this center.

- All of the Division's ongoing awards including those within the Clinical Research Program, the Biomedical Research Technology Program, the Laboratory Animal Sciences and Primate Research Program, and the Minority Biomedical Research Support Program, will be negotiated downward by an average of approximately 10 percent below recommended levels which will curtail the amount of resource support the Division is able to provide to the research community. This may delay progress on some research protocols, and will ultimately result in higher costs to the NIH research institutes when investigators begin including in their research project grants the cost of obtaining their own research resources and facilities to provide the resource capacities that DRR would no longer support. It will cost approximately $8.5 million to restore these awards to full funding.

- Support for the Biomedical Research Support Grant program will be eliminated in 1987. This program, which funded 557 research-intensive institutions in 1985 and 575 in 1986, advances and strengthens programs of biomedical research and health-related behavioral research by providing flexible funds, locally allocated. It will cost approximately $59.5 million to restore the Biomedical Research Support Grant program.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

Division of Research Resources

FY 1987 Budget — Page No.

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NATIONAL INSTITUTES OF HEALTH

Research Resources

For carrying out section 301 and Title IV of the Public Health Service Act with respect to research resources and general research support grants, [$305,696,000] *$234,192,000: Provided,* That none of these funds, with the exception of funds for the Minority Biomedical Research Support program, shall be used to pay recipients of the general research support grants program any amount for indirect expenses in connection with such grants. *(Department of Health and Human Services Appropriation Act, 1986.)*

NATIONAL INSTITUTES OF HEALTH

Research Resources

Amounts Available for Obligation 1/

	1985	1986	1987
Appropriation................	$304,025,000	$305,696,000	$234,192,000
Enacted administrative reduction..................	—	-29,000	—
Sequester order..............	—	-13,144,000	—
Proposed rescission..........	—	—	—
Subtotal, adjusted appropriation............	304,025,000	292,523,000	234,192,000
Comparative transfer to:			
Office of the Assistant Secretary for Health, for AIDS Projects..............	-2,802,000	-1,657,000 2/	
National Institute of Environmental Health Sciences for changes in Central Services financing mechanisms and formulas...................	714,000	—	—
National Library of Medicine for changes in Central Services financing mechanisms and formulas.............	1,086,000	—	—
Subtotal, adjusted budget authority........	303,023,000	290,866,000	234,192,000
Unobligated balance lapsing....	-384,000	-114,000	—
Total, obligations...........	302,639,000	290,752,000	234,192,000

1/ Excludes the following amounts for reimbursable activities carried out by this account: 1985 — $6,139,000; 1986 — $11,809,000; 1987 — $13,109,000, including $6,300,000 for AIDS projects.

2/ Comparative transfer at the appropriation level is $1,731,000.

Research Resources

Budget Mechanism

	1986 Appropriation 1/2/		1986 Available after Sequestering 1/3/		1986 Revised 1/3/		1987	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research grants:								
Research Centers								
Clinical research.............	78	$ 89,896,000	78	$ 86,031,000	78	$ 86,031,000	76	$ 86,082,000
Biomedical research technology	61	35,632,000	61	34,100,000	61	34,100,000	60	33,898,000
Laboratory animal sciences and primate research............	46	30,346,000	46	29,041,000	46	29,041,000	46	29,905,000
Subtotal, research centers..........	185	155,874,000	185	149,172,000	185	149,172,000	182	149,885,000
Other research								
Research Career Programs......	6	346,000	6	331,000	6	331,000	6	346,000
Biomedical research support...	720	95,500,000	713	91,393,000	713	91,393,000	154	32,883,000
Minority biomedical research support.....................	92	24,951,000	92	23,878,000	92	23,878,000	92	24,149,000
Other research related........	76	12,487,000	76	11,950,000	76	11,950,000	76	12,122,000
Subtotal, other research..	894	133,284,000	887	127,552,000	887	127,552,000	328	69,500,000
Total, research grants..........	1,079	289,158,000	1,072	276,724,000	1,072	276,724,000	510	219,385,000

Training								
Individual awards								
Noncompeting..................	3	84,000	3	81,000	3	81,000	3	84,000
Competing:								
New........................	--	---	--	---	--	---	--	---
Subtotal, individual......	3	84,000	3	81,000	3	81,000	3	84,000
Institutional awards:								
Noncompeting..................	36	991,000	34	948,000	34	948,000	16	453,000
Competing:								
Renewal.....................	--	---	--	---	--	---	19	538,000
New.........................	--	---	--	---	--	---	--	---
Subtotal, institutional ..	36	991,000	34	948,000	34	948,000	35	991,000
Total Training..................	39	1,075,000	37	1,029,000	37	1,029,000	38	1,075,000
Research and development contracts	6	5,189,000	6	4,965,000	6	4,965,000	6	5,031,000
Research management and support........................		8,514,000		8,034,000	FTEs 91	8,034,000	FTEs 91	8,701,000
TOTAL........................		303,936,000		290,752,000		290,752,000		234,192,000

1/ Reflects an enacted administrative reduction of $29,000.

2/ Reflects a comparable transfer of $1,731,000 to the Office of the Assistant Secretary for Health for AIDS research.

3/ Reflects a comparable transfer of $1,657,000 to the Office of the Assistant Secretary for Health for AIDS research and a consultant services (Section 515 of the Treasury-Postal Service Appropriation Act, 1985) withholding of $114,000.

NATIONAL INSTITUTES OF HEALTH

Research Resources

CROSSWALK - 1986 Appropriation 1/2/

(Dollars in Thousands)

MECHANISM

PROGRAM ACTIVITY	Research Grants		Training Programs		Research and Development Contracts	Research Management and Support	Total
	Research Centers	Other Research	Individual	Institutional			
Clinical research......	$89,896	$ 992			$ 65		$ 90,953
Biomedical research technology............	35,632	4,625			4,224		44,481
Laboratory animal sciences and primate research..............	30,346	7,216	$84	$991	900		39,537
Biomedical research support...............		95,500					95,500
Minority biomedical research support......		24,951					24,951
Research management and support...............						$8,514	8,514
Total............	155,874	133,284	84	991	5,189	8,514	303,936

1/ Reflects an enacted administrative reduction of $29,000.

2/ Reflects a comparable transfer of $1,731,000 to the Office of the Assistant Secretary for Health for AIDS research.

NATIONAL INSTITUTES OF HEALTH

Research Resources

CROSSWALK - 1986 Available After Sequestering 1/2/
and
1986 Revised Request

(Dollars in Thousands)

	MECHANISM						
	Research Grants		Training Programs				
PROGRAM ACTIVITY	Research Centers	Other Research	Individual	Institutional	Research and Development Contracts	Research Management and Support	Total
Clinical research......	$86,031	$ 949			$ 62		$ 87,042
Biomedical research technology............	34,100	4,426			4,042		42,568
Laboratory animal sciences and primate research..............	29,041	6,906	$81	$948	861		37,837
Biomedical research support...............		91,393					91,393
Minority biomedical research support......		23,878					23,878
Research management and support...............						$8,034	8,034
Total............	149,172	127,552	81	948	4,965	8,034	290,752

1/ Reflects an enacted administrative reduction of $29,000.

2/ Reflects a comparable transfer of $1,657,000 to the Office of the Assistant Secretary for Health for AIDS research and a consultant services (Section 515 of the Treasury-Postal Service Appropriation Act, 1985) withholding of $114,000.

NATIONAL INSTITUTES OF HEALTH

Research Resources

CROSSWALK - 1987 Congressional Justification

(Dollars in Thousands)

	MECHANISM						
	Research Grants		Training Programs		Research and Development	Research Management	
PROGRAM ACTIVITY	Research Centers	Other Research	Individual	Institutional	Contracts	and Support	Total
Clinical research......	$86,082	$ 960			$ 63		$ 87,105
Biomedical research technology............	33,898	4,408			4,095		42,401
Laboratory animal sciences and primate research..............	29,905	7,100	$84	$991	873		38,953
Biomedical research support...............		32,883					32,883
Minority biomedical research support......		24,149					24,149
Research management and support...............						$8,701	8,701
Total............	149,885	69,500	84	991	5,031	8,701	234,192

Research Resources

Summary of Changes

1986 Current estimated obligations..............................	$290,752,000
1987 Estimated obligations......................................	234,192,000
Net change...	-56,560,000

	1986 Base	Change from Base
Increases:		
A. Built-in:		
1. Within-grade pay increases.....	$3,864,000	+$60,000
2. Federal Employee Compensation Fund increase................	13,000	+2,000
3. FTS rate increase..............	64,000	+18,000
4. Payment for centrally furnished services...........	1,527,000	+366,000
6. Increased cost of supplies, materials, and other expenses	8,034,000	+311,000
Subtotal..........................		+757,000
B. Program:		
1. Research Centers:		
a. Clinical Research...........	86,031,000	+51,000
b. Laboratory Animal Sciences and Primate Research........	29,041,000	+864,000
2. Other research:		
a. Research career programs....	331,000	+15,000
b. Minority Biomedical Research Support............	23,878,000	+271,000
c. Other research related......	11,950,000	+172,000
3. Individual training awards.....	81,000	+3,000
4. Institutional training awards..	948,000	+43,000
5. Research and Development Contracts......................	4,965,000	+66,000
Subtotal..........................		+1,485,000
Total, increases.....................		+2,242,000

Summary of Changes--continued

	1986 Base	Change from Base
Decreases:		
A. Program:		
1. Research Centers:		
a. Biomedical Research Technology................	$34,100,000	-$202,000
2. Other research:		
a. Biomedical Research Support....................	91,393,000	-58,510,000
3. Research Management and Support......................	8,034,000	-90,000
Total decreases....................		-58,802,000
Total, net change..................		-56,560,000

Research Resources

Budget Authority by Activity

(Dollars in Thousands)

	1986 1/2/ Appropriation	1986 1/3/ Available After Sequestering	1986 1/3/ Revised		1987	
	Amount	Amount	FTEs	Amount	FTEs	Amount
Clinical research.......	$ 90,953	$ 87,042	—	$ 87,042	—	$ 87,105
Biomedical research technology............	44,481	42,568	—	42,568	—	42,401
Laboratory animal sciences and primate research..............	39,537	37,837	—	37,837	—	38,953
Biomedical research support...............	95,500	91,393	—	91,393	—	32,883
Minority biomedical research support......	24,951	23,878	—	23,878	—	24,149
Research management and support...............	8,514	8,034	91	8,034	91	8,701
Total obligations.....	303,936	290,752	91	290,752	91	234,192
Unobligated balance, lapsing...............	---	114	—	114	—	---
Total budget authority...........	303,936	290,866	91	290,866	91	234,192

1/ Reflects an enacted administrative reduction of $29,000.

2/ Reflects a comparable transfer of $1,731,000 to the Office of the Assistant Secretary for Health for AIDS research.

3/ Reflects a comparable transfer of $1,657,000 to the Office of the Assistant Secretary for Health for AIDS research and a consultant services (Section 515 of the Treasury-Postal Service Appropriation Act, 1985) withholding of $114,000.

Research Resources

Obligations by Object

	1985 Actual	1986 Estimate	1987 Estimate
Total number of full-time permanent positions..............................	79	79	79
Total compensable work years:			
Full-time equivalent employment.........	95	97	97
Full-time equivalent of overtime and holiday hours..........................	2	2	2
Average ES salary.......................	$66,232	$66,232	$66,232
Average GS grade........................	9.14	9.14	9.14
Average GS salary.......................	28,224	28,224	28,224
Average salary, grades established by act of July 1, 1944 (42 U.S.C. 207)...	35,361	35,361	35,361
Average salary of ungraded positions....	23,206	23,206	23,206
Personnel compensation:			
Full-time permanent..................	$ 2,841,000	$ 2,935,000	$ 3,088,000
Other than full-time permanent........	345,000	356,000	375,000
Other personnel compensation	125,000	129,000	137,000
Total, personnel compensation.......	3,311,000	3,420,000	3,600,000
Personnel benefits......................	429,000	444,000	462,000
Benefits for former personnel...........	7,000	7,000	7,000
Travel and transportation of persons....	172,000	172,000	180,000
Transportation of things................	11,000	11,000	11,000

Rent, communications, and utilities.....	206,000	255,000	304,000
Printing and reproduction..............	267,000	225,000	230,000
Other services:			
Project contracts.....................	5,103,000	4,965,000	5,031,000
Centrally furnished services..........	1,415,000	1,527,000	1,893,000
Other.................................	2,321,000	1,841,000	2,356,000
Supplies and materials.................	48,000	50,000	52,000
Equipment..............................	104,000	82,000	76,000
Grants, subsidies & contributions.......	289,245,000	277,753,000	219,990,000
Total..............................	302,639,000	290,752,000	234,192,000

Research Resources

Significant Items in House Appropriation Committee Reports

Item	Action Taken or To Be Taken
1986 House Report	
Regional Primate Research Centers	
1. "The Committee is becoming increasingly concerned over the level of funding for the primate centers located throughout the country. It is imperative that these centers maintain the highest standards in the care and treatment of animals. As a result, the Committee requests the Division of Research Resources (DRR) Director to prepare a plan to address the immediate and long range financial needs of these centers. The plan should be made available to the Committee before its consideration of the 1987 budget." (p. 76)	1. In response to this request, the Division has prepared a report entitled, "Report on Plan to Address the Immediate and Long Range Financial Needs of the Regional Primate Research Centers" which will be submitted to the Committee prior to its consideration of the 1987 budget.

Research Resources

Significant Items in Senate Appropriation Committee Reports

Item	Action Taken or To Be Taken
1986 Senate Report	
Regional Primate Research Centers	
1. "The Committee is becoming increasingly concerned over the level of funding for the primate centers located throughout the United States. It is imperative that these centers maintain the highest standards in the care and treatment of animals. As a result, the Committee instructs the Division of Research Resources (DRR) Director to provide the committee with a plan to address the financial needs of these centers." (p. 104)	1. In response to this request, the Division has prepared a report entitled, "Report on Plan to Address the Immediate and Long Range Financial Needs of the Regional Primate Research Centers" which will be submitted to the Committee prior to its consideration of the 1987 budget.

Research Resources

Authorizing Legislation

	PHS Act/ Other Citation	U.S. Code Citation	1986 Amt. Authorized	1986 Estimate	1987 Amt. Authorized	1987 Estimate
Research and Investigation......	Section 301	42§241	Indefinite	$302,907,000	Indefinite	$233,117,000
Division of Research Resources..	Section 479,480	42§287, 287a, 300aa, and 5§5332	Indefinite		Indefinite	
National Research Service Awards	Section 487	42§288	$244,000,000 1/	1,029,000	$260,000,000 1/	1,075,000
Total Budget Authority........				303,936,000		234,192,000

1/ This training authority is shared with other research training programs of the National Institutes of Health; the Alcohol, Drug Abuse, and Mental Health Administration; and the Health Resources and Services Adminstration.

Research Resources

Appropriations History

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation 1/
1978	102,230,000	145,095,000	145,095,000	145,095,000
1979	149,049,000	152,899,000	153,899,000	154,164,000
1980	154,302,000	169,199,000	164,000,000	169,196,000
1981	173,781,000	175,816,000	173,045,000	175,627,000
1982	168,839,000 2/	191,965,000	191,967,000	184,177,000
1983	191,024,000	227,642,000	199,967,000	213,912,000
1984	201,832,000	253,824,000 3/	230,031,000 3/	244,977,000 4/
1985	247,528,000	305,331,000 5/	305,298,000	303,023,000
1985 Proposed rescission	-250,000	---	---	---
1986	263,040,000	304,579,000 6/	305,739,000	303,936,000
1986 Sequester	-13,144,000			
1987	234,192,000			

1/ Reflects enacted supplementals, rescissions, and reappropriations.

2/ Reflects the September amendment; the original request was $191,863,000.

3/ Excludes $720,000 in NRSA training programs not considered.

4/ Includes $708,000 for NRSA training programs authorized under a Continuing Resolution.

5/ Excludes $775,000 in NRSA training programs not considered.

6/ Excludes $1,075,000 in NRSA training programs not considered.

Research Resources

Justification

	1986 Appropriation Amount	1986 Available After Sequestering Amount	1986 Revised FTEs	1986 Revised Amount	1987 FTEs	1987 Amount
Clinical research.....	$ 90,953,000	$ 87,042,000	--	$ 87,042,000	—	$ 87,105,000
Biomedical research technology............	44,481,000	42,568,000	--	42,568,000	—	42,401,000
Laboratory animal sciences and primate research..............	39,537,000	37,837,000	—	37,837,000	—	38,953,000
Biomedical research support...............	95,500,000	91,393,000	—	91,393,000	—	32,883,000
Minority biomedical research support......	24,951,000	23,878,000	—	23,878,000	—	24,149,000
Research management and support...........	8,514,000	8,034,000	91	8,034,000	91	8,701,000
Total................	303,935,000	290,752,000	91	290,752,000	91	234,192,000

General Statement

The Division of Research Resources (DRR) provides for the development, support and administration of resources which are essential for maintaining the quality of the environment in which modern biomedical research is conducted. DRR is the component of the National Institutes of Health (NIH) charged with the responsibility for identifying and providing needed research resources to investigators at biomedical research institutions throughout the country. The Division achieves its mission by awarding grants, contracts, cooperative agreements, and research training grants for a wide variety of research resources and institutional needs, and by providing technical expertise, information exchange, and research opportunities to investigators.

The Division will continue to meet the needs of research investigators in 1987. Researchers need instruments that can image cancer cells in three dimensions, microsensors that can monitor heart rhythms in vivo or monitor newborn infants susceptible to sudden infant death syndrome, mass spectrometers that can provide rapid automated analysis of several hundred stable isotope samples per day, or a computer system that can analyze EKG recordings in conjunction with a study of drugs under development to control cardiac arrhythmias. Clinical investigators need specialized clinical environments where they can apply research advances such as recombinant DNA-produced insulin and growth hormone to the treatment of human health problems, or where they can conduct clinical trials of new drugs. Laboratory animals are used for multiple studies including testing the safety and effectiveness of diagnostic and treatment techniques prior to clinical trials in humans.

Through its five extramural programs the Division provides support for such resources, for manpower development and for flexible funds to institutions for equipment and facilities, pilot research, support of new investigators, and for interim and emergency research needs. The Clinical Research Program supports the development and maintenance of specialized clinical research environments within larger hospitals. The Biomedical Research Technology Program provides biomedical researchers access to the latest technologies from the physical sciences, mathematics, and engineering. The Laboratory Animal Sciences and Primate Research Centers (LASPRC) Program supports projects which focus on the most effective use of animals in research and the development of appropriate animal models; further, support is provided for the National Primate Research Centers and a number of unusually valuable animal colonies as well as for essential animal facility improvement awards. The Biological Models and Materials Resources activity within the LASPRC is developing the uses of cell systems, lower organisms and nonbiological systems as models in biomedical research. The Biomedical Research Support Grant (BRSG) Program enables institutions to conduct research programs more efficiently and effectively, using local decision-making to determine how best to use the formula grant funds (for equipment and facilities, pilot research, support of new investigators, and/or for emergency research needs). The Biomedical Research Support Shared Instrumentation Grant Program provides funds for the purchase of up-to-date research instruments that can be shared by groups at PHS-grant supported biomedical researchers. The Minority Biomedical Research Support Program supports both the participation by ethnic minority students and faculty in the biomedical sciences and health professions and development of the research and research training capabilities of the institutions that serve minority populations.

Overall Budget Policy

The 1987 budget request for the Division of Research Resources is $234,192,000; $56,560,000 below the comparable 1986 level. This level of support will enable the Division to maintain much of its ongoing research resources effort in 1987 while reducing overall federal outlays and assisting the Administration in meeting the goals of the Balanced Budget and Emergency Deficit Control Act of 1985.

The 1987 budget request assumes that 4.3 percent of the funds appropriated in 1986 will be sequestered, in accordance with the Balanced Budget and Emergency Deficit Control Act of 1985. This will result in downward negotiations of the direct costs of all awards in 1986 by an average of approximately 8 percent from study section recommended amounts, as well as a reduction in the Division's administrative management and support costs. These program reductions in 1986 will be reflected in 1987 by decreases in commitment levels required in 1987.

DRR will also negotiate the direct cost of all awards in 1987 by an average of approximately 9 to 10 percent from study section recommended amounts. In 1987, 182 research centers will receive support from the Division, three fewer than in 1986, and 154 shared instrumentation grants are expected to be funded, 2 fewer than in 1986. With these exceptions, the 1987 budget request will allow the Division to maintain support to the same numbers of awards as in 1986, including 6 research career awards; 92 minority biomedical research support grants; 9 animal facility improvement awards; 46 other research grants; 21 small business innovative research grants; and 6 research and development contracts.

Indirect costs associated with most research grants will be reduced; the decrease will be focused on the administrative costs of the grantee institutions.

The Biomedical Research Support formula grant activity will be eliminated in 1987. This reduction is proposed in order to permit NIH to continue funding 18,000 investigator-initiated research project grants at a time when reductions are necessary in order to attain the goals of the Balanced Budget and Emergency Deficit Control Act of 1985. Maintenance of a stabilized base of investigator-initiated research project grants will ensure that researchers with meritorious new ideas will have an opportunity for successfully competing for funds.

The 1987 budget request includes $1.0 million to continue to address the repair and renovation needs of the Primate Research Centers: to repair roofs at several of the centers, improve sewage disposal systems, renovate ventilation and sanitation equipment, provide additional caging and cage washing equipment, and replace obsolescent central research equipment.

The animal facilities improvement program will be continued in 1987 at a funding level of $3,981,000, which is expected to support 9 awards--the same number as in 1986.

The Division recognizes the importance of stabilizing its support for research instrumentation and will maintain approximately the same level of instrumentation support in 1987 as in 1986 in the Shared Instrumentation Grant Program. The 1987 budget request includes $31,383,000, which will support approximately 154 Shared Instrumentation grants, two fewer than in 1986.

The 1987 request for research training supports one more trainee in 1987 than in 1986. The Division will support 35 institutional trainees and three individual fellowships.

The 1987 request excludes $6,300,000 for AIDS, which are under the single AIDS appropriation in the Office of the Assistant Secretary for Health. Comparable amounts for 1986 are $1,657,000; and for 1985, $2,802,000.

The 1987 budget request for Research Management and Support is $8,701,000; $553,000 more than the comparable 1986 level. This level reflects an increase of $757,000 for mandatory administrative cost increases, offset by savings achieved from management improvements and program decreases.

Program Accomplishments

In 1985, the Division of Research Resources initiated a new activity of animal facility improvement awards to help institutions upgrade animal facilities and develop centralized programs of animal care in support of their biomedical research programs. A major objective is to enable institutions to comply with the Animal Welfare Act and the Department's policies on the care and treatment of laboratory animals. More than 100 applications were received for this new program in 1985.

The Division has been active in AIDS and AIDS-related research. In fiscal years 1985 and 1986, eighteen of the general clinical research centers (GCRCs) provided the research setting for studies of opportunistic infections in immunocompromised patients, AIDS epidemiology, therapeutic interventions for the primary disease as well as for opportunistic infections such as cytomegalovirus, and studies of immune system function in AIDS patients. The GCRCs enable clinical researchers to respond quickly to research opportunities in areas of public health emergencies, provide adequate facilities, research beds, equipment and research personnel as necessary to support demand. Scientists at the New England Primate Research Center discovered the first T-cell trophic HTLV III-like virus to be found in monkeys. The virus causes a fatal disease in rhesus monkeys that closely resembles human AIDS, except that its clinical course is much shorter. This model is being used for the study of antiviral and therapeutic agents as well as for developing and testing candidate vaccines for AIDS.

The Division organized the new Biological Models and Materials Resources Section within the Laboratory Animal Sciences and Primate Research Program. The mission of this unit is to develop and support cell systems, lower organisms, and nonbiological models which serve as important resources to the biomedical research community. Previously, there had been no single component at NIH that provided overall noncategorical support or coordination for biological models and materials resources.

Following extensive study and consultation, the Minority Biomedical Research Support Program has developed two new initiatives. One enables biomedical research participation by undergraduate colleges with substantial enrollments of minority students that were not being funded by the MBRS Program. The other, designed for minority institutions with more biomedical research faculty and updated research equipment, focuses on developing faculty and interdepartmental collaboration around specific research themes. This "Thematic Program Grant" is intended as a transitional step toward applications for regular NIH grant support by the target institutions.

A milestone in structural biology was reached in 1985 with the determination of the structure of a human rhinovirus by investigators from Purdue University. Rhinoviruses are responsible for the common cold. The data collection for this X-ray crystallographic study was carried out at the synchrotron Resource at Cornell University supported by the Biomedical Research Technology Program.

Using instruments awarded through the Biomedical Research Support Shared Instrumentation Grant program, investigators at the University Health Science Center at Dallas have made major advances in understanding the genetic background, biochemistry and regulation of human cholesterol metabolism; two recent Nobelists for Medicine, were integral to the groups of scientists involved.

Research Resources

AIDS Research

The Division of Research Resources (DRR) supports efforts in the area of Acquired Immunodeficiency Syndrome (AIDS), Simian Acquired Immunodeficiency Syndrome (SAIDS), and AIDS-related research activities. Clinical studies of AIDS are being conducted within the General Clinical Research Centers (GCRC) Program. In fiscal years 1985 and 1986, eighteen of the general clinical research centers were involved in AIDS research. Center investigators conducted research in areas such as opportunistic infections in immunocompromised patients, epidemiological studies of AIDS patients, therapeutic interventions for the primary disease as well as for opportunistic infections such as cytomegalovirus, and studies of immune system function in AIDS patients. Center investigators were also involved in several collaborative studies.

The general clinical research centers will continue to direct their research capability toward AIDS studies in 1987 as local opportunities arise. The GCRCs are especially appropriate because they can provide flexibility for clinical researchers to respond quickly to research opportunities in areas of public health emergencies. The centers provide appropriate facilities, research beds, equipment and research personnel as necessary to support the increased investigator demand for well-equipped clinical environments in which to conduct AIDS research. Specifically, the centers can cooperate in clinical trials initiated by the NIH categorical institutes, in trials of new therapies initiated by the private sector, and can participate in PHS efforts to obtain new epidemiological information and compare AIDS with other immunodeficiency diseases.

The New England and California Primate Research Centers have become recognized leaders in research on immunodeficiency diseases of nonhuman primates caused by retroviruses. In searching for the cause of immunodeficiency diseases that were occurring in the Center's animal colony, scientists at the New England Center discovered the first T-cell trophic HTLV III-like virus to be found in monkeys. The virus causes a fatal disease in rhesus monkeys that closely resembles human AIDS, except that its clinical course is much shorter. This model will be very useful for the study of antiviral and therapeutic agents as well as for developing and testing candidate vaccines for AIDS. The emphasis of work at the California Center has been on preventing, treating, and eradicating simian acquired immunodeficiency syndrome where this disease has been a serious clinical problem. This Center has been successful in developing a vaccine that has been shown to fully protect monkeys against challenge with virulent virus. With the development of necessary virological and immunologic capabilities, techniques, and collaboration, the Washington, Oregon, Yerkes and Delta Primate Research Centers have discovered retroviruses in their colonies like those found at the New England Center. They are also proceeding with studies of viral characterization and pathobiology that have already yielded unique and exciting results. Finding that many sooty mangabey monkeys circulate an HTLV III-like virus, without showing any sign of immunodeficiency disease, has been just one of these.

Research Resources

Clinical Research

1987 Authorization: Indefinite.

Budget Authority:

1986 Appropriation	1986 Available After sequestering	1986 Revised Estimate	1987	Increase or decrease
$90,953,000	$87,042,000	$87,042,000	$87,105,000	+ $63,000

Purpose and Method of Operation

The Clinical Research Program provides specialized environments and resources necessary for the conduct of high quality clinical research studies, through a network of General Clinical Research Centers (GCRCs) throughout the country. These centers provide the necessary clinical facilities that enable clinical investigators to study normal and disease processes *in vivo*. A typical hospital ward cannot provide the controlled environment required for complex clinical research, since its primary mission is to provide care and treatment. Perceiving this need for a specialized clinical research environment and for increased patient-oriented research, the U.S. Senate, in 1959, urged special studies on humans, leading to the establishment of the first General Clinical Research Centers. Through clinical research, physicians learn more about the prevention, treatment and control of human disease and can apply the technological and therapeutic advances of basic research to improved patient care.

Specific goals of centers funded by the program are:

- to learn more about normal and abnormal body function and about the cause, progression, prevention, control and cure of human diseases;
- to provide an optimal setting for controlled investigation by clinical scientists supported by the NIH and other organizations;
- to encourage increased collaboration among investigators in the basic and clinical sciences;
- to encourage, develop and maintain a national corps of expert clinical investigators; and
- to provide resources that allow advances in basic scientific knowledge to be translated into methods for improved patient care.

Investigators at the GCRCs have contributed greatly to improved patient care by developing timely applications of new basic research findings. Current studies range from use of noninvasive diagnostic imaging techniques and sophisticated metabolic analyses to detect heart and blood diseases to the use of tissue-compatible drug-infusion devices to treat cancer and diabetes, to the testing of treatment modalities for patients with AIDS. Research projects conducted at the clinical research centers are funded by the categorical Institutes of the NIH, by other agencies of the Department of Health and Human Services, by research foundations and societies, and by industry. Efforts have increased in recent years to develop formal evaluations of the program's contributions to specific advances in medicine and more effectively transmit the knowledge gained from this research to the medical community.

Conducting a successful clinical research protocol is highly dependent on the research setting. Thus, the centers are designed to provide the best possible environment, including the personnel and technical tools, in which researchers can provide superior care for research patients while acquiring new health knowledge. A "typical" clinical research center can accommodate both inpatients and outpatients, and supports a medical program director, 12 nurses, 3 dietitians, 2 laboratory technicians, and one or two administrative personnel. The average center size is about 8 beds (range, 4 to 30). Centers often contain treatment rooms, a core laboratory, a diet kitchen, patients' lounge space, a nurses station, a conference room, and outpatient space. These Centers account for 87 percent of the extramural patient care funds provided by NIH for investigating clinical applications of laboratory findings. Over 175,000 inpatient days are supported by the Program annually, as well as 120,000 outpatient visits. The GCRC program pays the hospital costs of all patients admitted to the centers solely for research purposes. About 30 percent of patients participating in research projects require hospitalization for diagnosis or treatment; these patients are billed for this portion of their hospital stay, usually through third-party insurers.

In order to meet the increasing needs of GCRC investigators for management and analysis of data obtained in clinical research, a computer-based system called "CLINFO" was developed and has been in use on the centers since 1979. Currently 40 CLINFO systems serving 49 GCRCs are being supported. These 40 CLINFO sites have been linked during the past year through an electronic mailnet. The mailnet allows investigators at General Clinical Research Centers to exchange information, reports and clinical research data. Several studies are underway which utilize the mailnet in multicenter clinical trials.

The CLINFO system has become an integral part of many GCRCs, and is used daily for a wide variety of purposes. It has been used to collect and analyze data from multi-center clinical trials involving large numbers of patients studied over long periods of time. For example, it is an important element in a study of diagnosis and treatment modalities for immunodeficiency syndromes. CLINFO is also being used to analyze retrospectively patient histories, clinical data, laboratory data and treatment regimens. CLINFO allows retrieval of patient data in various formats and over various time periods.

As a national resource for the conduct of clinical research, the Centers also provide an ideal facility for clinical research training of medical students, house staff, physicians in postdoctoral positions, and nursing and dietitian students. The Clinical Associate Physician (CAP) Program is a subactivity within the GCRC Program which supports young clinical investigators--physicians who have completed fellowship training—for up to two years, to enable them to begin clinical research careers under the tutelage of senior GCRC investigators. During 1985, the Program funded 47 CAP positions, 13 of which were new positions. Since the CAP Program's inception in 1974, 177 CAP awards have been made; 130 individuals have completed their research training, and so far, 57 of them have been successful in obtaining NIH research support. All but 14 of the former CAPs are in academic positions.

Some examples of recent scientific accomplishments on the centers follow.

A new test of peripheral vision, acuity perimetry, has been developed at the University of Iowa GCRC for the early detection of visual loss from glaucoma. The ability of the patient to resolve fine detail is measured at different locations in the field of vision. This ability is impaired in early glaucoma before loss of vision is detected by conventional visual field testing. It is anticipated that acuity perimetry will become a practical test for detection of early glaucomatous loss of vision in patients who have elevated intraocular pressures or abnormal-appearing optic nerves.

Current medical practice largely disregards the time of day at which a drug is administered. GCRC-based experiments at the University of Minnesota indicate, however, that the timing of administration of adriamycin and cisplatin, the two most commonly used anticancer drugs in the United States, substantially influences their toxicity. In patients treated on a GCRC for advanced ovarian cancer, toxicity was markedly diminished when adriamycin was given in the morning and cisplatin in the evening, rather than on other schedules. Extracorporeal and implantable programmable drug delivery systems may soon make the accurate timing of drug administration much more practical, allowing the use of clinical "chronotherapy" to optimize the therapeutic effects of these drugs and minimizing their toxicity.

Increases in blood calcium concentrations from many causes lead to blood vessel contractions which can increase blood pressure and damage the kidneys. Studies conducted at the University of Southern California GCRC in normal volunteers show that even small rises in serum calcium stimulate production by the blood vessel wall of a compound called prostacyclin, which helps maintain normal pressure. These studies demonstrate a new blood pressure regulatory system protecting against the damaging effects of hypercalcemia.

Some patients with diabetes mellitus may develop a life-threatening increase in blood potassium. Control of blood potassium is a complicated process in which the production of an adrenal hormone, aldosterone, is required to act on the kidney to regulate potassium excretion in the urine. Aldosterone production is in turn controlled in great part by a kidney enzyme, renin. New findings at the University of Southern California GCRC indicate that potassium elevation in diabetic patients comes about because a defect in the kidneys causes a decreased production of the active form of renin, possibly because of a deficiency of the fatty acid derivative prostacyclin. The unraveling of the problem of control of blood potassium may greatly aid in the care of diabetic patients.

Persistent functional abnormalities of the adrenal glands have been found in almost all patients with AIDS studied so far at the center at San Francisco General Hospital. The relationship of these abnormalities to the syptoms and signs of AIDS, many of which resemble those of adrenal insufficiency, is under intensive study.

Prostatic cancer is a common disease in aging men. Its cause is unknown, but androgenic hormones secreted by the testes contribute to development of the tumor. It has been observed that brothers of men who developed the cancer before age 63 have a four-fold higher risk for this tumor than men of similar age in the general population, and that men at risk for the disease tend to have low normal plasma levels of testosterone. Current studies at the University of Utah GCRC indicate that men at risk for the cancer actually produce increased testosterone each day, but metabolize it more rapidly. These metabolites of testosterone are more potent than testosterone itself in stimulating growth of the prostate gland. These observations suggest that men at risk for development of prostatic cancer may have an inherited alteration of testosterone metabolism predisposing them to the occurrence of this tumor at a relatively early age.

Early data from studies at the Albany Medical College GCRC suggest promising results with a new vaccine for Hemophilus influenza B, the most common cause of bacterial meningitis in infants and young children. If this vaccine is successful, over 20,000 cases of meningitis could be prevented annually.

A longitudinal study of 150 type II diabetics at the Johns Hopkins University GCRC has revealed that hypertension and angiotensin II levels are important risk factors for diabetic blood vessel deterioration, especially that which causes degenerative renal disease. The data suggest that control of hypertension in diabetes might markedly slow the development of end-stage renal disease, especially if therapy involved the use of converting enzyme inhibitors, which block angiotensin action. If so, the number of diabetics requiring dialysis because of diabetic nephropathy might be markedly reduced. Since approximately 25 percent of all patients currently entering dialysis with end-stage renal disease have diabetic nephropathy, the findings of this study are of great potential public health interest.

There is increasing evidence that better blood sugar control, such as that produced by multiple daily injections of insulin or a continuous subcutaneous insulin infusion by means of a wearable pump, can slow the onset of complications of diabetes. Also, an insulin-containing nasal spray has been found in an outpatient study at the Boston University GCRC to be effective, practical, and well tolerated over the long-term for control of blood sugar. The results suggest that intranasal insulin has potential as an adjunct to subcutaneous insulin in the therapy of insulin-dependent diabetes, especially for patients who are unable or unwilling to give themselves injections several times a day.

Multiple sclerosis is the most common degenerative disease of the nervous system in young adults in this country, affecting about 250,000 patients. It inflicts numerous physical and psychological difficulties on the victims and their families, and is estimated to cost about $1.8 billion a year in medical, hospital, and rehabilitation expenses, and in lost income. A four-year pilot study at the center at Albert Einstein College of Medicine has revealed that Copolymer I, a synthetic substance imitating in certain respects a natural constituent of nerve tissue, reduces the number of attacks of the disease and arrests the progression of disability.

Rationale for the Budget Request

The 1987 budget request for the Clinical Research Program is $87,105,000, an increase of $63,000 over the comparable 1986 level. In 1986, the Clinical Research Program will maintain support to 78 general clinical research centers. In accordance with the Balanced Budget and Emergency Deficit Control Act of 1985, funds available for the Clinical Research Program in 1986 have been reduced by 4.3 percent. This will result in downward negotiations of the direct costs of all awards in 1986 by an average of approximately 8 percent from study section recommended levels.

Funds have been provided to support 76 centers in 1987, two fewer than in 1986. The Division will continue to reduce overall costs in 1987 through recovery of third party insurance payments for hospitalized patients, through the use of more outpatient research studies, and by carefully negotiating the cost of each remaining center downward by an average of approximately 10 percent from study section recommended levels. Through these methods, and by reducing the indirect costs associated with all GCRC awards in 1987, the Division will be able to maintain a strong clinical research resource for the biomedical research community.

As a result of research initiatives by the NIH in areas of national concern, the translation of basic scientific knowledge into clinical applications, and procedures which can be used in the delivery of health care and in the prevention of disease, there is expected to be a continued demand for use of GCRC beds by research investigators supported by NIH. Because of the high initial expense of clinical research facilities and the increasing cost of hospital care, more and more investigators are expected to seek out the shared, stable environment already existing at the GCRCs. The 76 GCRCs will strive to meet this demand and preserve the availability of research beds and the related laboratory and skilled personnel resources for use by biomedical investigators.

Impact Data	1986 Appropriation	1986 Available after sequestering	1986 Revised estimate	1987
Res. centers				
Number	78	78	78	76
Amount	$89,896,000	$86,031,000	$86,031,000	$86,082,000
Other res.				
Number	5	5	5	5
Amount	992,000	949,000	949,000	960,000
Res. & Dev. Contracts				
Number	1	1	1	1
Amount	65,000	62,000	62,000	63,000
Total	90,953,000	87,042,000	87,042,000	87,105,000

Research Resources

Biomedical Research Technology

1987 Authorization: Indefinite.

Budget Authority:

1986 Appropriation	1986 Available After sequestering	1986 Revised Estimate	1987	Increase or decrease
$44,481,000	$42,568,000	$42,568,000	$42,401,000	-$167,000

Purpose and Method of Operation

The Biomedical Research Technology (BRT) Program was initiated in 1962. Since that time, the BRT Program has modified and expanded its scope. The Program now places greater emphasis on regional and national sharing of resources and resource technologies. Each resource site also provides collaborative research opportunities, training, an information center, and other services. Today, the Program focuses on applications of knowledge engineering, information technology, biomedical engineering and digital technology for biomedical and clinical research programs, and technologies for the study of biomolecular and cellular structure and function.

In the computer area, the Program has developed a number of important resources including: expert systems for medical diagnosis and for assisting physicians with the management of patients enrolled in cancer chemotherapy protocols; computer graphics techniques for modeling molecular structures of proteins; quantitative imaging technology for analysis of three-dimensional images of organs, tissues and cells; specialized systems for diagnosing and assessing eye damage, aiding hearing, and modeling of neural processes; and the PROPHET System, a large, integrated computer system for management and analysis of research data. In the area of technologies for the study of biomolecular and cellular structure and function, the Program has developed and used mass spectrometry and nuclear magnetic resonance techniques for structure determination and analyses of biological materials; million volt electron microscopy for study of cellular structure in three dimensions and scanning transmission electron microscopy for analyzing biomacromolecules in the cell *in situ*.

The following are illustrations of research accomplishments in the applications of knowledge engineering, information technology, biomedical engineering and digital technology for biomedical and clinical research programs.

It is estimated that there are 40,000 new cases of idiopathic scoliosis (curvature of the spine) a year, affecting primarily young women at the onset of puberty. This disease has grave implications for the health, social adjustment and, in a significant portion of the cases, the actual survival and longevity of the patients. In a study mentioned in prior statements, scientists collaborating with the Rockefeller University Microprocessor Biomedical Research Technology Resource have developed an automated portable, posture-training device that incorporates precise behavioral principles and enables therapeutic training to be given unobtrusively in the patient's normal environment throughout the entire day. Using results from a highly successful series of field trials on 35 patients in the United States and Germany over periods of up to three years, the investigators are currently working on an improved model based on these field studies. The new model will provide higher reliability, have greater potential for miniaturization and have the ability to continuously adapt to the patient's postural behavior. It is planned to license this model for worldwide distribution. The prospects are excellent that this medical device will make a major contribution toward alleviating this significant health problem.

To set safety standards for the environment and human consumption, quantitative information on toxic and carcinogenic effects of chemicals are needed. The National Biomedical Simulation Resource at Duke University is helping researchers develop new computer techniques to aid in predicting effects of chemicals on human health. Both the process of absorption into the human body and the mechanisms of toxicity and carcinogenesis are highly complex. The study is greatly aided by the use of computer simulation. For example, a computer program which accounts for blood flow to the lungs or other organs can predict how a toxic chemical will be distributed in the body, when it is breathed in or swallowed. The Resource is developing more powerful computer procedures which will aid in screening new compounds for toxicity by comparing their chemical and physical properties with known toxic chemicals that have similar structures. Such computer programs make possible a partial extrapolation of information from animals to humans and to human populations with special local problems.

The three-dimensional anatomy of cell structures and interactions have become increasingly important in biology and medicine. However, obtaining this information with the detail needed has been exceedingly difficult and time consuming. Neuroanatomists need to know the connectivity of nerve nets and the size and location of cell clusters which produce particular hormones in order to relate these data to the physiology, behavior, and diseases of the nervous system. In the past, cancer pathologists have not made significant use of three-dimensional information on tumor structure or vascularization for purposes of diagnosis or establishing a prognosis. It is important to explore the usefulness of such information. In order to obtain such three-dimensional information, "reconstruction" must be made from many serial microscopic images. Considerable help has been obtained in the past by using computers to record features seen in individual photographs but the process becomes practical only when the processes of extracting relevant features can be automated. The Molecular Mechanics and Neuro-Anatomy Computer Resource at Columbia University has developed automated feature extraction procedures, using new computer hardware for image processing and applying sophisticated pattern recognition techniques. The new system is now becoming functional and is beginning to be used in experiments with brain and tumor sections. Its potential is most promising.

The PROPHET System is a unique national computer network used by approximately 1,000 biomedical research scientists for data management, graphics, statistical analysis, mathematical and molecular modeling, and for nucleotide and amino acid sequencing. Data sharing and research collaboration between scientists working at widely separated geographical locations are greatly facilitated. Since its inception in 1972 the PROPHET network has made use of centralized time-sharing, accessed by users via telephone lines. A "new generation" PROPHET network is being developed by the Biomedical Research Technology Program, based upon state of the art computer technology and "architecture".

The new PROPHET incorporates the full range of PROPHET software in a microcomputer which would be located in a scientist's laboratory. The software will be written in a "portable" language thereby allowing it to operate on a variety of microcomputers. Access will be via a range of intelligent workstations from the most powerful graphic workstations to relatively inexpensive and readily available personal computers. The capabilities thus provided will satisfy virtually all the data handling needs of the majority of biomedical research workers. This new design will permit the dissemination of PROPHET to a much larger number of NIH grantees.

The following are illustrations of research accomplishments in technologies for study of biomolecular and cellular structure and function.

Juvenile onset diabetes mellitus is a systemic disorder caused by an insulin deficiency and a large excess of glucagon, another pancreatic hormone; the disease is characterized by irregularities in sugar and fatty acid metabolism. Investigators at the Michigan State University Mass Spectrometry Facility recently completed a comparative study of the levels of about 250 organic acids in diabetic patients and control subjects using combined gas chromatography-mass spectrometry methods. Diabetic urines contained two unusual acids, possibly the breakdown products of the amino acid threonine. These newly observed metabolites may be important measures of protein breakdown in skeletal muscle under conditions of insulin deficiency. The Michigan State scientists investigated this hypothesis by using isotopically enriched threonine provided by the National Stable Isotope Resource, also funded by DRR. The results expand our understanding of the metabolic abnormalities associated with juvenile diabetes and provide the basis for further investigations of amino acid metabolism in this disease.

A milestone in structural biology was reached in 1985 with the determination of the structure of a human rhinovirus by investigators from Purdue University. Rhinoviruses are responsible for the common cold. The data collection for this X-ray crystallographic study was carried out at the DRR-supported synchrotron Resource at Cornell University. The project took several years to complete and required both the high intensity X-rays provided by the synchrotron and the enormous computer power provided by the Purdue University supercomputer for solution. The structure is remarkably similar to that of human poliovirus and more surprisingly to some plant viruses. It would be extremely interesting if viruses fall into a series of families with similar morphologies and perhaps modes of action; structure often relates to function, and research on such families would be important in understanding viral diseases.

The Mass Spectrometry Resource at Washington University School of Medicine has pioneered in the quantitative application of mass spectrometry to clinical research problems, particularly in the area of metabolism. In collaboration with investigators from Harvard and MIT, quantitative estimates of essential amino acid metabolism were conducted. Labelled amino acids were provided by the National Stable Isotopes Resource and clinical resources were provided by the Washington University General Clinical Research Center, also funded by DRR. Oxidative loss of amino acids was estimated using the loss of breath $^{13}CO_2$ when a labelled essential amino acid tracer is injected intravenously. The approach was tested using normal volunteers adapted to various intake levels of leucine, valine, lysine and threonine; in each instance net oxidative loss was quantified after injection of the respective amino acid tracer. The results indicate minimal requirements for these amino acids to be well above the "established" recommended intakes based on N-balance values. In a related study, it was found that exercising subjects oxidize the "daily requirement" of leucine within two hours. These studies have wide-ranging implications. Estimates for minimal requirements for protein are used as guidelines for nutrition programs throughout the world. Established recommendations for human daily protein intake for both the resting and physically active state may well have to be revised upward in the future.

Applications of magnetic resonance imaging and spectroscopy to health areas are expanding rapidly. A number of projects from the University of Pennsylvania Magnetic Resonance Resource illustrate this progress. Magnetic resonance imaging and spectroscopy was used to evaluate the metabolism of phosphate in infants with neuroblastoma that had infiltrated the liver. The investigators were able to differentiate between tumors having different growth patterns and monitor the response to treatment. In animal model studies they have obtained images of rodent brains showing locations of lithium ion. Lithium is an important component in the treatment of mental illness. The ability to locate lithium in intact animal brains will expand research opportunities in these areas, particularly when combined with other approaches to examination of brain function such as positron emission tomography.

Rationale for the Budget Request

The 1987 budget request for the Biomedical Research Technology Program is $42,401,000, a decrease of $167,000 below the comparable 1986 level. In accordance with the Balanced Budget and Emergency Deficit Control Act of 1985, funds available for the Biomedical Research Technology Program in 1986 have been reduced by 4.3 percent. This will result in downward negotiations of the direct costs of all awards in 1986 by an average of approximately 7 to 8 percent from study section recommended levels. In 1986, the Biomedical Research Technology Program will maintain support to 61 resource center grants, 24 resource-related research project grants, small grants and conference grants, approximately 15 small business innovative research grants, and 3 research and development contracts.

The 1987 budget request will enable the Division to maintain support to 60 resource center grants, one fewer than in 1986, 24 resource-related research project grants, small grants and conference grants, 15 small business innovative research grants, and 3 research and development contracts. The Division will carefully negotiate the cost of each of the 60 centers downward by an average of approximately 10 percent below study section recommended levels. In addition, indirect costs associated with all BRTP awards will also be reduced in 1987.

The Program will continue to address the instrumentation needs of the biomedical research community by providing advanced instrumentation at biomedical research technology centers, by supporting research on instrument development or new research techniques, and by supporting short-term training in the application of research technologies using high technology instrumentation.

Special emphasis will be directed at providing support to regional facilities for the development and application of in vivo Nuclear Magnetic Resonance (NMR) spectroscopy and new imaging methodologies which are expected to serve both basic and clinical research scientists and should greatly facilitate the creative application of these powerful new tools to biomedical research problems.

Impact Data	1986 Appropriation	1986 Available after sequestering	1986 Revised estimate	1987
Computer resources	$15,815,000	$15,135,000	$15,135,000	$15,075,000
Biomedical engineering	4,263,000	4,080,000	4,080,000	4,064,000
Biological structure and function	24,403,000	23,353,000	23,353,000	23,262,000
Total	44,481,000	42,568,000	42,568,000	42,401,000
Res. centers				
Number	61	61	61	60
Amount	35,632,000	34,100,000	34,100,000	33,898,000
Other res.				
Number	39	39	39	39
Amount	4,625,000	4,426,000	4,426,000	4,408,000
Res. & Dev. Contracts				
Number	3	3	3	3
Amount	4,224,000	4,042,000	4,042,000	4,095,000
Total	44,481,000	42,568,000	42,568,000	42,401,000

Research Resources

Laboratory Animal Sciences and Primate Research

1987 Authorization: Indefinite. 1/

Budget Authority:

1986 Appropriation	1986 Available After sequestering	1986 Revised Estimate	1987	Increase or decrease
$39,537,000	$37,837,000	$37,837,000	$38,953,000	+$1,116,000

1/ Authorization for research training totals $260,000,000 in 1987 for NIH, ADAMHA and HRSA.

Purpose and Method of Operation

The Laboratory Animal Sciences and Primate Research (LASPR) Program supports resource activities which make use of laboratory animals and other biological models in order to make their use more efficient and more effective. This is accomplished through grants which provide base support for the overall resources and a broad spectrum of multicategorical types of biomedical research conducted in seven Regional Primate Research Centers. The LASPR Program also supports diagnostic laboratories, research manpower development in laboratory animal sciences, special nonanimal biomedical models, the improvement of laboratory animal facilities, and other activities which undergird NIH categorical programs.

The Program advises on the use of biomedical models which may limit or even replace the use of research animals and assists the Office of the Director, NIH, in the development of guidelines for the humane care and use of animals in research. The LASPR Program serves as liaison to various animal welfare and professional scientific societies interested in the care of laboratory animals. The three components of this Program are Regional Primate Research Centers, Laboratory Animal Sciences and Biological Models and Materials Resources Programs.

Regional Primate Research Centers Program

The seven Regional Primate Research Centers were established by the National Institutes of Health to provide specialized resources (physical facilities, technology, professional and technical staff, and a variety of nonhuman primate species) and appropriate research environments for a broad range of basic and applied biomedical investigations. The Centers are located in the states of California, Oregon, Washington, Wisconsin, Massachusetts, Georgia and Louisiana. Each Center is closely associated with a major host academic institution where its core scientists hold joint appointments.

In addition to core staff scientists, research teams at each Center include collaborative and affiliated investigators from other institutions who use the Center's laboratories and primate resources. Visiting scientists from other institutions throughout the United States and other countries may receive formal appointments for specified periods at the Centers. Collectively, the seven Centers provide resources and services for more than 800 investigators who use the nonhuman primate as the most appropriate model for investigations on important human health problems.

Special attention continues to be given to a five-year Center modernization and improvement program that began in 1984. The program was initiated to address the need for extensive renovations and repairs to physical facilities that are presently more than 25 years old, as well as to modernize animal care and laboratory equipment. With significant contributions from the Division of Research Resources, host institutions and other sources, considerable progress has been made. Improvements that have been accomplished enabled two of the Centers to become accredited by the American Association for Accreditation of Laboratory Animal Care (AAALAC) in the last two years. Thus, six of the seven PRC's are now accredited. Major improvements underway at the seventh should make its accreditation possible in the next two years.

During the past year, the Primate Research Centers have continued to make important contributions in numerous research areas such as infectious diseases, neurosciences, toxicology, immunology, reproductive biology, nutritional and metabolic diseases and environmental health sciences. The following represent examples of research advances during the past year typical of the Centers' present accomplishments.

The New England and California Centers have become recognized leaders in research on immunodeficiency diseases of nonhuman primates caused by retroviruses. In searching for the causes of immunodeficiency diseases that were occurring in the Center's animal colony, scientists at the New England Center discovered the first T-cell trophic HTLV III-like virus to be found in monkeys. The virus causes a fatal disease in rhesus monkeys that closely resembles human AIDS, except that its clinical course is much shorter. While becoming a useful model for AIDS studies, this disease has also resulted in the loss of approximately 500 macaque monkeys. This model will be very useful for the study of antiviral and therapeutic agents as well as for developing and testing candidate vaccines for AIDS. The emphasis of work at the California Center has been on preventing, treating, and eradicating simian acquired immunodeficiency syndrome where this disease has been a serious clinical problem. This Center has been successful in developing a vaccine that has been shown to fully protect monkeys against challenge with virulent virus. With the development of necessary virological and immunologic capabilities, techniques, and collaboration, the Washington, Oregon, Yerkes and Delta Centers have discovered retroviruses in their colonies similar to the retrovirus found at the New England Center. They are also proceeding with studies of viral characterization and pathobiology that have already yielded unique and exciting results. The recent finding that many sooty mangabey monkeys are infected with an HTLV III-like virus, without showing any sign of immunodeficiency disease, has been just one of these.

In another area of research, scientists at the New England Center, using the latest molecular biological techniques, genetically manipulated a virus, Herpesvirus saimiri, to produce growth hormone. The virus, which causes latent infections in squirrel monkeys, readily infected cells and produced large amounts of growth hormone for long periods of time. This finding could have practical importance for industrial applications. The work also has good potential for correcting inborn errors of metabolism. Through genetically engineering herpesvirus vaccines, and using them as carriers to insert particular genes into intracellular machinery, it may be possible to produce biological products such as growth hormone in people or animals, who could not produce them on their own.

At the Washington Center, significant work continues to demonstrate the impact on the fetus of alcohol consumption during pregnancy. This work shows that learning deficits can be detected in infant monkeys whose mothers experience blood alcohol levels of 240 mg./dl. and greater at intervals during pregnancy, not unlike weekly "binges." Concurrent work is allowing compilation of morphologic data on the development of the fetal and infant brain that may shed light on how outside factors influence fetal development and subsequent learning. A new Center resource, the automated quantitative microscopy laboratory, whose development was sponsored with a DRR shared instrumentation grant, will substantially accelerate the pace at which both normal and abnormal brain development can be studied. A computer-based morphometric system is being programmed to digitize projection drawings from serial brain sections and to calculate volumes of specific structures and the volume of the whole brain. Growth curves have been plotted from 105 to 190 days of age, and show that maximal growth of the brain occurs before birth. Determining the critical periods of development of the primate brain, and influences of outside factors have become much easier because of this new technology.

New antiviral compounds are being studied at the Delta Center. Two such fluorinated pyrimidine compounds were studied in African green monkeys infected with simian varicella (monkey pox) virus. Both drugs, given orally beginning 48 hours after virus inoculation, protected monkeys from manifestations of typical disease including mortality, rash and viremia. One of the drugs, given as late as seven days after experimental infection, showed clear signs of antiviral activity. Based on this work, the drug was recommended to treat a serious outbreak of monkey pox with associated high mortality that occurred in the rhesus monkey colony of a large commercial testing laboratory. Although 17 of 442 monkeys had died earlier, there were no further deaths following treatment, despite the fact that clinical cases continued to occur. These results provide good evidence that these drugs will be useful for the treatment of human diseases caused by herpesviruses. Some toxicity has already been seen in human clinical trials that make it uncertain whether these particular drugs will be licensed for further use in humans. However, promising lines of investigation have been opened for developing and similarly evaluating drug analogs that retain these desirable antiviral properties, but may be better tolerated clinically.

Laboratory Animal Sciences Program

The Laboratory Animal Sciences Program (LASP) assists institutions in developing and improving animal resources for biomedical research and training through the award of research, resource and improvement grants. Program areas include support for research related to important laboratory animal disease problems, animal colonies which serve as national resources for biomedical research, studies directed at finding animal models which are needed for research on human diseases, institutional animal resource improvement projects to help upgrade animal facilities and develop centralized programs of animal care, laboratories for the diagnosis and control of diseases of laboratory animals, and research training of specialists in the field of laboratory animal medicine.

Resource-related research grants are awarded to improve the health and availability of research animals and to provide needed information to manage animal resources effectively. The majority of these projects involve investigation of the etiology, pathogenesis, and control of laboratory animal disease problems. For example, current projects include the diagnosis and control of mammalian encephalitozoonosis, control of respiratory mycoplasmosis in rodents, establishing resistance and susceptibility factors to Sendai virus infection in mice, studying the pathogenesis of mouse hepatitis virus in laboratory mice, and development of a live vaccine for the control of pasteurellosis in rabbits. The last project is of particular significance, because pasteurellosis is an important complicating disease of experimental rabbits.

The major objectives of animal model and special colony projects are: 1) to define, characterize, and utilize the relevant biological attributes of selected animals which display potential for use in biomedical research; and 2) to establish, improve, or expand special colonies of well-characterized animals which are of proven value for biomedical research, but which are not generally available from other sources. For example, several marine invertebrate projects involving loliginid squids and octopuses are designed to develop a system and methodology for large-scale culture of these species for biomedical research. Because cephalopods are the only invertebrates with a closed circulatory system and a highly vascularized brain, they are particularly suitable for studies of the correlations between behavior and the nervous system. Octopuses are important in learning experiments, as they have short- and long-term memory stores. Their vertebrate-like eyes have also been used for studies of phototransduction, corneal regeneration and neural pathways.

Native species of Octopus are not readily available in the United States. Support for a project was initiated to develop methods for large-scale culture of Octopus, in order to make them available on a scheduled basis to investigators in the United States. Excellent progress has been made during the initial project period. Five species of Octopus were raised through their life cycles, including two species which had never previously been raised.

A relatively new resource activity is located at the Jackson Laboratory. Entitled, "Cryopreservation of Murine Germplasm", the long-term objective of this project is to establish a bank of frozen mouse embryos to preserve mutants and strains of mice that are valuable to many fields of research. In many cases, cryopreservation will allow a reduction in the number of size of colonies maintained by conventional breeding procedures and will also serve to retard genetic drift. Freezing techniques, using eight-cell embryos, frozen at a controlled rate and stored in liquid nitrogen, are now well established. More than 425,000 embryos have been frozen and stored from approximately 450 different strains since the project's inception 4 years ago. To date, over 40 strains have been terminated from active breeding because they have been safely preserved. Seven strains were reconstituted successfully last year for research use, including one strain that was recovered to replace breeding stock that were lost.

Three nonhuman primate resources (in addition to the seven Regional Primate Research Centers) are supported by the Program. These projects help ensure a stable supply of those species of nonhuman primates which are required by NIH grantees for their research in such important areas as organ transplantation, reproductive physiology, and vaccine testing. The projects include production colonies of baboons at the Southwest Foundation, squirrel monkeys at the University of South Alabama, and two species of Galago (bushbabies) at Duke University. A Primate Supply Information Clearinghouse, located at the University of Washington, is also supported to facilitate maximum research utilization of primates already in this country. The Clearinghouse matches requests for primates, primate tissues, and related services with investigators and breeding colonies who have these items available. This activity saved many thousands of dollars compared with the purchase and conditioning costs of newly-imported primates, and also reduced the number of animals used for research purposes.

The objectives of resource laboratories are to provide for improved laboratory animal health programs through appropriate surveillance activities and investigation of naturally-occurring disease and other laboratory animal problems, to support studies resulting in new information on diseases of laboratory animals and their etiology, to aide in the elucidation of new animal models of human disease, and to develop resources for research and training. Although diarrhea is the second most important disease in laboratory rabbits complicating research, the cause has been difficult to determine and represents a common problem for animal diagnostic laboratories. It is noteworthy that viruses of the rotavirus group are an important cause of diarrhea in other animals and humans. Accordingly, one resource laboratory has investigated whether there is any association of rotaviruses with disease in rabbits, and whether the infection in rabbits represents a potentially productive animal model for the infection in humans. Approximately 90% of the adult rabbits tested had antibodies to rotavirus. Rabbits are born with maternal (transplacental) antibody which disappears between one and two months of age and the rabbits are naturally infected soon thereafter. This pattern of infection is similar to that seen in humans, thus the rabbit may prove to be a valuable model of human rotavirus infection.

Institutional animal resource improvement projects are awarded to help institutions upgrade their animal facilities and develop centralized programs of animal care in support of their biomedical research programs. A major objective is to enable institutions to comply with the Animal Welfare Act and the Department's policies on the care and treatment of laboratory animals. The Fiscal Year 1985 appropriation provided a major increase in funding for animal resource improvement projects. Institutions were allowed to request up to $500,000 for alterations and renovations (A&R) on a 50:50 matching basis, plus needed equipment. A total of 100 applications were received requesting $38.6 million, including $16.2 million for equipment and $20.8 million for A&R. The latter category was matched by a $29.5 million institutional commitment. Seventy-four applications were recommended for approval with budgets totaling $20.64 million. Twenty-three one-year awards were made, totalling $8.568 million.

Training in laboratory animal medicine is intended to prepare individuals to provide professional care of the many species of laboratory animals, to manage central animal resources, and to give special assistance to investigators through knowledge of laboratory animal biology and understanding of research methods. In addition, the trainees are prepared to participate in the teaching of graduate students and young investigators and to pursue their own research interests either as independent investigators or as members of a research team. Currently available figures indicate that 220 trainees and fellows have completed training since the inception of training grants and fellowships in laboratory animal science and medicine. The majority (132) are serving as directors or staff members of a vivarium; 71 are engaged in teaching and research or are obtaining additional training; and 17 are in public health, private practice or are retired. Retention in the field of laboratory animal medicine has been excellent, emphasizing the career orientation provided by such training and the continuing need for and opportunities available to such individuals.

Biological Models and Materials Resources

The Biological Models and Materials Resources Section (BMMRS) was created on February 21, 1985, as an integral unit of the Animal Resources Program. The mission of the new Section is to develop and support cell systems, lower organisms, and nonbiological models which serve as important resources to the biomedical community. The Section is addressing the need to explore and support the utilization of nonmammalian models in biomedical research. Primary guidance for formulation of the new Section's programs is derived from an evaluation of the use of model systems in biological research completed in 1985 by the National Academy of Sciences under a contract funded by the National Institutes of Health entitled "Models for Biomedical Research: A New Perspective". The Academy reported on the relevance of various models for biomedical research, paying particular attention to invertebrates, nonmammalian vertebrates, in vitro techniques (cell and tissue culture), and nonbiological approaches (mathematical and computer-assisted systems). The report recommends that:

1) NIH strive to make favorable systems readily available to the research community by providing support to supply organisms for research, maintaining stock centers for mutant strains and cell lines, facilitating access to computer programs for biomedical modeling, maintaining data bases like those for protein and DNA sequences, and providing long-term support for collections of monoclonal antibodies.

2) NIH consider supporting development of new model systems for specific research areas.

3) NIH consider encouraging interest in nonmammalian systems through fellowships, symposia and direct support of model developments.

4) NIH investigate the matrix of biological knowledge concept as a potential tool for biomedical research.

Since the publication of the Report, the following activities have taken place:

1) Two workshops to examine the feasibility of formalizing the concept of the matrix of biological knowledge as a tool for the research community.

2) A third workshop to determine the needs for biomaterials resources; determine the range of systems identifiable as biomaterials resources; provide a definition of biomaterials, useful to the new Section in planning its activities; consider selection or establishment of priorities among identified, meritorious, and needed biological materials resources; and suggest means for identifying biological resource needs.

3) Provision of full or partial support to several important resources including the American Type Culture Collection (ATCC); the MIT Cell Culture Center; the Caenorhabditis elegans Genetics Center; the National Diabetes Research Interchange; and the Repository of Human DNA Probes and Libraries.

Rationale for the Budget Request

The 1987 budget request for the Laboratory Animal Sciences and Primate Research (LASPR) Program is $38,953,000, an increase of $1,116,000 over the comparable 1986 level. In accordance with the Balanced Budget and

Emergency Deficit Control Act of 1985, funds available for the LASPR Program in 1986 have been reduced by 4.3 percent. This will result in downward negotiations of the direct costs of all awards in 1986 by an average of approximately 8 to 10 percent from study section recommended levels.

The 1987 budget request will enable the Division to maintain support to 7 regional primate research centers, 39 laboratory animal sciences center grants, approximately 20 resource-related research project grants and conference grants, 6 research career awards, 9 animal facility improvement awards, 3 small business innovative research grants, and 2 research and development contracts. Thirty-five postdoctoral institutional trainees and 3 individual fellowships will be supported in 1987. Stipend levels for trainees and fellows will remain at the same level as in 1986. The Division will carefully negotiate the cost of each of the 7 primate research centers downward by an average of approximately 8 percent, and each of the 39 laboratory animal sciences center grants by an average of approximately 7 percent from study section recommended levels. In addition, indirect costs associated with all LASPR program awards will also be reduced in 1987.

Within the funds available for the Primate Research Centers, $1,000,000 will be available in 1987 to continue to address the repair and renovation needs of the Primate Centers. This initiative began in 1984 to upgrade the animal facilities to maintain standards for accreditation by the American Association for Accreditation of Laboratory Animal Care. The $1,000,000 in 1987 will be used for major roof repairs at several centers, improve sewage disposal systems, renovate ventilation and sanitation equipment, provide additional caging and cage washing equipment, and replace obsolescent central research equipment.

The animal facilities improvement grant program is funded at a level of $3,981,000 in 1987. It is expected that 9 animal facility improvement awards will be made in 1987.

The 1987 request will allow the LASPR program to maintain its research efforts directed toward the development of high quality animal resource programs, the further development of animal models and colonies, the establishment of better breeding methods, and the provision of diagnostic laboratories, reference centers and the primate information clearinghouse. In addition, the LASPR program will explore further the scientific potential for the development of additional research models such as invertebrates, non-mammalian systems, cell systems, etc. and new applications for biological materials.

Impact Data	1986 Appropriation	1986 Available after sequestering	1986 Revised estimate	1987
Primate res. centers	$23,589,000	$22,575,000	$22,575,000	$23,344,000
Lab. animal sciences	14,698,000	14,066,000	14,066,000	14,389,000
Biological Models and Materials Dev.	1,250,000	1,196,000	1,196,000	1,220,000
Total	39,537,000	37,837,000	37,837,000	38,953,000
Res. centers				
Number	46	46	46	46
Amount	30,346,000	29,041,000	29,041,000	29,905,000
Other res.				
Number	38	38	38	38
Amount	7,216,000	6,906,000	6,906,000	7,100,000
Training				
Number	39	37	37	38
Amount	1,075,000	1,029,000	1,029,000	1,075,000
Res. & Dev. Contracts				
Number	2	2	2	2
Amount	900,000	861,000	861,000	873,000
Total	39,537,000	37,837,000	37,837,000	38,953,000

Research Resources

Biomedical Research Support

1987 Authorization: Indefinite.

Budget Authority:

1986 Appropriation	1986 Available After sequestering	1986 Revised Estimate	1987	Increase or decrease
$95,500,000	$91,393,000	$91,393,000	$32,883,000	-$58,510,000

Purpose and Method of Operation

The Biomedical Research Support (BRS) Program is designed to strengthen institutional research in the health sciences. It consists of three subactivities, the Biomedical Research Support Grant Program, the Shared Instrumentation Grant Program and the Minority High School Student Summer Research Apprenticeship Program. Each of these subactivities is described below.

Biomedical Research Support Grant

The Biomedical Research Support Grants (BRSGs) advance and strengthen the medical and health-related research programs of academic and scientific institutions by providing flexible funds to be used by the institution. More specifically, the objectives are (1) to cultivate scientific excellence through building institutional strengths, (2) to contribute to the stable support and development of institutional programs, (3) to enable an institution to provide for institutional needs not provided by other funding mechanisms, (4) to meet emerging opportunities in research and pursuit of new ideas, and (5) to enable earlier recognition and support of scientific talent.

The BRSG program permits the grantee institution to make its own judgments and decisions at the local level over the emphasis, direction, content, and quality of its biomedical research efforts.

The flexible nature of BRSG funds enables an institution to initiate support for pilot research which enables investigators to explore new research ideas to test their validity and to provide preliminary findings necessary to support research project grant applications. In addition, the BRSG program provides unforeseen requirements for projects supported from other sources such as: repair or replacement of research equipment; increasing the research skills of investigators to take advantage of newly developed techniques or to pursue new directions in their research;

interim support of research personnel, equipment, and supplies to maintain research programs during temporary lapses in project grant support. It also provides initial research support for new investigators and investigators newly relocated at an institution. The BRSG program also provides centralized research facilities by providing sophisticated equipment to investigators that cannot be justified by any single project and by providing research services and specialized expertise in areas such as animal care, computer technology, and instrument design.

The major impact of the BRSG program is establishment and maintenance of a stable research environment that provides maximal effectiveness and efficiency in the production of high quality biomedical and behavioral research with a minimum investment of BRSG funds. Consequently, the full scope of PHS supported biomedical research is stabilized, balanced, and strengthened.

BRSG funds have been used to support or augment a number of research studies that have direct application to human health problems such as the following:

Duchenne muscular dystrophy (DMD) is probably the most common X-linked disorder in man, affecting one in 4,000 males, the disease being transmitted by carrier females. Sisters of affected boys have a 50 percent risk of being carriers, but there has been no reliable test for prenatal diagnosis or for carrier females. The locus for DMD is in the middle of the short arm of the X chromosome Xp21. In a collaborative effort involving several east-coast institutions, the successful cloning of a DNA fragment that detects a deletion which is in or very near the DMD gene was recently reported. This is a major breakthrough that forms the basis for much more accurate detection of females carrying the gene. It will also help in the understanding of this lethal disease.

The importance of vitamin K in prevention of "hemorrhagic disease of the newborn (HDN)" is well understood and it is general practice for infants born in hospitals to receive an intramuscular supplement of this vitamin. However, in recent years reports of HDN have been increasing in the United States, presumably due to the increasing popularity of home births and the resulting lack of supplementation with vitamin K at birth, and the increasing popularity of breast feeding which may not provide adequate levels of the vitamin. Because both vitamins A and K are particularly important to newborns, both must be provided in adequate levels immediately during the postnatal period, and because infants are generally born with low stores of these vitamins, those that are born prematurely or with any form of disease are especially susceptible to deficiencies of these vitamins and their status should be monitored particularly carefully. However, vitamins K and A are present in plasma and other tissues in very trace amounts and the presence of large amounts of other chemically- similar lipids has made reliable quantitation of the vitamins very difficult in the past. Accordingly, little is known of endogenous levels of vitamins K and A in human milk or in plasma and other tissues of human infants. BRSG funds are being used by a children's hospital on the west coast to develop new laboratory procedures for analysis of vitamins K and A that are sensitive, reproducible and require very small sample volumes.

Researchers at a West Coast institution have developed a painless, non-invasive technique for disintegrating kidney stones using laser generated shock waves. This new technique is a great improvement that is considered to be much safer than other methods for treating this extremely painful condition. BRSG funds supported the initial fundamental experiments necessary to define the technique and establish its feasibility. The basic research has been directly applied by colleagues in the institution's Department of Urology using animal models. Private industry has provided additional funding, and the University has licensed the technology.

Minority High School Student Reseach Apprentice Program

The purpose of the Minority High School Student Research Apprentice (MHSSA) Program is to provide minority high school students with a meaningful experience in various aspects of health-related research in order to stimulate their interest in careers in science.

Eligible institutions are those that were awarded grants during the latest complete Federal fiscal year from either the Biomedical Research Support Grant (BRSG) Program or the Minority Biomedical Research Support (MBRS) Program.

Students who are selected by the applicant institution, are eligible for support under this program if they identify themselves as minority (i.e., Black, Hispanic, American Indian, Alaskan native, Pacific Islander, or Asian); are U.S. citizens or have a permanent visa; and are enrolled in high school.

The mechanism of support for this program is an NIH grant-in-aid. Support is provided at a level of $1,500 for each apprentice position allocated. No indirect costs are paid. Within the $1,500 per student allocation, funds are used for student salaries, supplies, extending the research experience, or if adequate funds exist, for an additional apprentice. The Program Director is responsible for recruitment and selection of the apprentices and assignment of each to an investigator. Basis for recruitment and selection of students emphasize students' motivation, ability and scholastic aptitude and accomplishments. In addition, consideration is given to science teachers' recommendations and, where applicable, the degree of parental commitment. Students are assigned to investigators involved in health-related research who are committed to developing in the high school students both understanding of the research in which they participate and the technical skills needed.

Shared Instrumentation Grant Program

Contemporary research would not be imaginable without today's modern tools of science. Very recent advances in the design of equipment have provided new opportunities for an integrated approach to genetic analysis and engineering. These methods have very important applications to the studies of human diseases, gene structure and expression, oncogenes and tumor biology, growth regulatory factors, peptide hormones and molecular immunology - studies that are currently being carried out by PHS - supported investigators.

The objective of the BRS-Shared Instrumentation Grant (SIG) program is to make available large, expensive instrumentation (in the $100,000 to $300,000 cost range) to institutions for groups of PHS-funded investigators on a shared-use basis. In five years of operation, the program has received an average of 200 applications per year. Through FY 1985, the program has made 400 awards for a total of 69.2 million dollars. Over 3,000 NIH-supported investigators have benefitted from this program. This enthusiastic response indicates the need, and satisfying this need will lead to important collaborative interactions for medical researchers.

New technical capabilities continue to become available for advanced biomedical research. In the past year, the BRS-SIG program has received applications for newly developed instruments such as in vivo nuclear magnetic resonance spectrometers, multi-wire detectors for x-ray crystallography and neuromagnetometers. These applications are in addition to more commonly requested instrumentation which include electron microscopes, mass spectrometers, image analysis and computer graphics systems, cell sorting facilities and an array of instruments for peptide synthesis and DNA sequencing. With the increased use of microprocessors, the development of new technologies and the demand to update equipment, institutions will always be faced with pressures to improve instrumentation, especially that shared by a broad group of users.

The following scientific accomplishments illustrate the value of shared instrumentation facilities, and show how interactions among research groups with complementary capabilities can combine efforts and skills to lead to important contributions to challenging research problems.

Instruments awarded to the University Health Science Center at Dallas since 1982 have enhanced the research progress of more than 30 NIH supported investigators. Two investigators have utilized these instruments to accomplish a major achievement in human medicine. One of the investigators used a cell sorter to develop a fluorescence method to permit reliable quantitation of the number of low density lipoprotein (LDL) receptors on human lymphocytes to permit direct diagnosis of familial hypercholesterolemia. A DNA synthesizer was used by the second investigator to make mixed probes for isolation of cloned cDNA's for the LDL receptor and to synthesize DNA sequences for (HMG-COA) reductase, the enzyme critical for the regulation of the cholesterol level in the body.

In 1985, an amino acid analyzer was used by the second investigator to obtain sequence information on the LDL receptor protein and by the first investigator to generate peptides and antisera to map the functional domains of HMG COA reductase.

A gas-phase protein sequencer is currently being used by the second investigator to carry out detailed structure-function studies on the LDL receptor protein. In October 1985 these two investigators were jointly awarded the 1985 Nobel Prize in medicine for their research on the LDL receptor protein and its role in the uptake of nutritional and regulatory molecules, the role the receptor plays in regulation of cholesterol metabolism and for their studies on how the LDL receptor is responsible for the common human disease called familial hypocholesterolemia.

A computerized flow cytometer was awarded to the Immunopathology Unit of the Massachusetts General Hospital in Boston. Investigators at this institution had a very pressing demand for analysis of circulating cells from AIDS patients while conducting research under a grant from the National Cancer Institute. Under this grant, one hundred homosexual men are being studied prospectively every three months for two years using a panel of monoclonal antibodies that detect T-cell subsets and other surface markers. An evaluation of the immunological parameters is needed to establish the sensitivity and specificity of these cells in identifying immunologic abnormalities associated with AIDS. This instrument has the advantage of being a closed system easily sterilized.

The SIG Program made instrumentation awards to the Laboratory for Cell Analysis, operated by the Department of Laboratory Medicine of the University of California, San Francisco. This unique facility was established to provide the latest technologies of cell analysis and sorting to cell biologists and medical scientists throughout the University of California system. Instruments available at the San Francisco facility include a cell sorter, a laser-activated device for analyzing and separating fluorescent-labelled cells and an image analyzer that contains a video system permitting computer analysis of cell and tissue images. These instruments are being used in NIH supported research projects to conduct a study of retroviruses as mutagens and the origins of oncogenes; to conduct a study of interferon and immunologic functions in Down syndrome; and to study how interferon produced by the immune system affects cancer cells.

Rationale for the Budget Request

The 1987 budget request for the Biomedical Research Support Program is $32,883,000, a decrease of $58,510,000 below the comparable 1986 level. The 1986 level for the BRS Program has been reduced by 4.3 percent in accordance with the Balanced Budget and Emergency Deficit Control Act of 1985.

The Biomedical Research Support formula grant activity will be eliminated in 1987. This reduction has been proposed by the administration in order to permit NIH to continue to support 18,000 investigator-initiated research project grants, at a time when reductions are required in order to meet the goals of the Balanced Budget and Emergency Deficit Control Act of 1985. Maintenance of a stabilized base will ensure that researchers with meritorious new ideas will have an opportunity for successfully competing for funds. In order to provide continued support to research investigators at those institutions most heavily engaged in biomedical research, institutions will be encouraged to require more sharing of resources and facilities, allow more release time for investigators to conduct pilot research activities, initiate institutional development programs for new investigators, and seek additional funds from within the institution and other private sources.

The 1987 budget request for the Shared Instrumentation Grant (SIG) Program is $31,383,000, an increase of $1,009,000 over the comparable 1986 level. This program is designed to replenish and maintain the large scale, expensive, shared instrumentation necessary for biomedical research. The Division expects to make approximately 154 SIG awards in 1987, 2 fewer than in 1986, owing to the increased costs of purchasing high technology instrumentation.

The Minority High School Summer Research Apprentice (MHSSA) Program will be continued in 1987 at a level of $1,500,000, the same level as in 1986. At this level of funding, the Division will be able to provide 8 weeks summer support to 1,000 high school students at approximately 270 research institutions throughout the country. The purpose of the apprentice program is to provide meaningful experience in various aspects of health-related research in the expectation that some of the apprentices will decide to pursue higher education and eventually careers in health research.

Impact Data	1986 Appropriation	1986 Available after sequestering	1986 Revised estimate	1987
Biomedical res. support	$62,260,000	$59,519,000	$59,519,000	—
Minority high school student summer res. apprenticeship	1,500,000	1,500,000	1,500,000	$1,500,000
Shared instrumentation grants	31,740,000	30,374,000	30,374,000	31,383,000
Total	95,500,000	91,393,000	91,393,000	32,883,000
Other res.				
Number	720	713	713	154
Amount	95,500,000	91,393,000	91,393,000	32,883,000
Total	95,500,000	91,393,000	91,393,000	32,883,000

Research Resources

Minority Biomedical Research Support

1987 Authorization: Indefinite.

Budget Authority:

1986 Appropriation	1986 Available After sequestering	1986 Revised Estimate	1987	Increase or decrease
$24,951,000	$23,878,000	$23,878,000	$24,149,000	+$271,000

Purpose and Method of Operation

The Minority Biomedical Research Support (MBRS) Program was established in 1972 to address the limited representation of minorities in the ranks of biomedical research scientists. Increasing the numbers of minority biomedical researchers is the major goal of the program. MBRS grants support the participation of undergraduates, graduates and faculty in biomedical research. The program focuses on colleges (two year and four year), universities and health professional schools in which 50 percent or more of the students are classified as minorities (Black, Hispanic, American Indian, Pacific Islander-Asian). Other institutions, with substantial minority enrollments (but less than 50 percent) that have a history of and/or demonstrate special commitment and assistance to minority students and faculty are also eligible to participate in the program. At developing institutions and those where the primary mission is teaching, the MBRS Program provides faculty participants released time to provide opportunity to engage in research in which they can involve their students. At such institutions, equipment, supplies and renovation of facilities to accommodate research are also supported by the program. Faculty at eligible majority institutions with substantial minority enrollments (less than 50 percent) who are active in research as evidenced by a record of research publications and research grant support, can also participate in MBRS programs. This is accomplished by providing support to students who are involved in ongoing research projects.

Most of the institutions who have participated in the program have had "Traditional" MBRS Program Grants. This mechanism provides support for an administrative component and a group of individual research projects that may involve numerous faculty from a variety of disciplines, along with student participants. The overall objective is to develop an institutional capability in biomedical research, thus providing the opportunity for faculty to engage in research, and the students to choose and pursue biomedical research careers.

Undergraduate College Research Participation Awards are limited to eligible undergraduate colleges (two and four year) and involve pilot projects, a variety of "enrichment" activities to motivate students to choose biomedical research careers, as well as possible support for individual pilot research projects for faculty.

Thematic Grant Awards are limited to current MBRS grantees that are considered developing institutions with 50 percent or more minority enrollment and that award the doctorate degree (Ph.D., M.D., D.D.S., D.V.M.) in the biomedical disciplines. These awards were initiated in 1985 to provide support for a group of investigators who are developing research organized around a particular theme.

Supplemental Awards for Shared Instruments are for purchases of research equipment and instruments that ordinarily could not be justified for a single project, costing $25,000 to $135,000. To be eligible, an institution must have a current MBRS grant.

The first MBRS grant awards, totaling $2 million, were made in 1972 to 38 institutions. By 1985, the number of grantees had increased to 95 and the appropriation for the program had increased to $24.9 million.

Institutions currently supported include 5 two-year colleges and 46, 22, and 18 institutions which offer as their highest degree baccalaureate, masters, and doctorate degrees, respectively. Five of the institutions serve primarily American Indians, 55 serve primarily Blacks, 8 serve primarily Puerto Ricans, 15 serve other Hispanics, and 2 serve Hawaiians. The remainder serve a mixed population of minorities in large metropolitan areas and the Southwest.

In Fiscal Year 1985, the Program supported positions for 1,109 undergraduate students, 415 graduate students, and 778 faculty. They were involved in 647 different research projects, including 234 projects cofunded by ten NIH institutes, the National Institute of Alcohol Abuse and Alcoholism and the National Institute of Mental Health. Areas of research ranged from clinical studies on hypertension to recombinant DNA technology. The diverse nature and sophistication of this research are in marked contrast to studies conducted during the early years of the MBRS Program. Approximately 7,500 minority students have participated in the MBRS Program since 1972. Of the nearly 5,500 students receiving baccalaureate degrees, about 80 percent have been accepted to graduate schools, medical, dental, and other health professional schools, or have entered other health-related careers.

The National Academy of Science has identified a total of 199 former MBRS students as having received Ph.D.s from all Ph.D.-granting institutions reporting to NAS. In a preliminary report, the American Dental Association has identified 94 former MBRS students who have been awarded the D.D.S. and about 53 who are currently enrolled in dental schools. Similarly, a preliminary report by the American Association of Medical Colleges lists 617 former MBRS students who have received the M.D. and 580 who have enrolled in medical schools, but have not yet received their medical degree.

Research Accomplishments:

An investigator at the State University of New York/College at Old Westbury has determined that two species of (bryozoa), mosslike sea animals that attach to submerged surfaces much like barnacles do, contain compounds with antibacterial and antitumor properties. The yet-to-be characterized alkaloid compounds inhibit the growth of gram-positive bacteria such as Staphyloccus aureus, which is known to be a causative agent of toxic shock syndrome.

Assays show that bryozoan extracts suppress cell division, suggesting that the unknown active agents might check the cellular proliferation that is characteristic of cancer. Studies to determine the structural composition of these compounds are now underway. Although some bryozoan species inhabit pristine waters, many thrive in polluted marine environments. This ability, combined with the fact that the organisms are unaffected by the high concentrations of bacteria flourishing in their colonies, suggests that bryozans have specially adapted mechanisms that favor their widespread survival. This combination suggests that the animals produce and secrete "chemical products that allow them to master their environment." Such chemicals could be potentially useful for medical or other human purposes.

In other tests, it was found that the active agent in the extract from one of the bryozoans arrested the embryonic development of the sea urchin Arbacia punctulata. Results from this test, which is used as a preliminary screen for antitumor activity, demonstrated that the agents inhibit mitosis. These findings raised the prospect that extracts contain a novel compound that potentially could be used in the treatment of cancer patients.

At Florida A&M University, an investigator whose research is supported in part through the MBRS Program, has reduced or eliminated the systemic toxic side effects of prednisolone, a currently used anti-inflammatory and anti-allergic drug, by modifying the chemical structure. The university has applied for 16 patents on these new drugs.

Not only has MBRS support played a significant role in faculty and student development, but it has also played a major role in institutional development. For example, because of the increase in the number and quality of faculty research competence, the College of Pharmacy at Florida A&M University initiated, on September 1, 1984, the first Ph.D. program in the institution's 98 year history.

Rationale for Budget Request

The 1987 budget request for the Minority Biomedical Research Support (MBRS) Program is $24,149,000, an increase of $271,000 over the comparable 1986 level. In accordance with the Balanced Budget and Emergency Deficit

Control Act of 1985 funds available for the MBRS Program in 1986 have been reduced by 4.3 percent. This will result in downward negotiations of the direct costs of all awards in 1986 by an average of approximately 5 percent from study section recommended levels.

The 1987 budget request will enable the Division to maintain support to 92 MBRS awards, the same number as in 1986. The Division will carefully negotiate the cost of each of the 92 MBRS awards downward by an average of approximately 8 percent from study section recommended levels. In addition, indirect costs associated with all MBRS awards will also be reduced in 1987.

Co-funding by the categorical institutes of the NIH and by the National Institute of Mental Health and the National Institute of Alcohol Abuse and Alcoholism in 1987 will continue. This activity helps expand the number of research projects that can be supported. In 1987, the categorical institutes of the NIH have budgeted $9,493,000 for co-funding support of the MBRS Program; thus bringing the total anticipated funding level by NIH in 1987 to $33,642,000, an increase of $267,000 over the 1986 current level.

Impact Data	1986 Appropriation	1986 Available after sequestering	1986 Revised estimate	1987
Other res.				
Number	92	92	92	92
Amount	$24,951,000	$23,878,000	$23,878,000	$24,149,000
Total	24,951,000	23,878,000	23,878,000	24,149,000

Research Resources

Research Management and Support

1987 Authorization: Indefinite.

Budget Authority:

1986 Appropriation	1986 Available After sequestering	1986 Revised Estimate	1987	Increase or decrease
$ 8,514,000	$ 8,034,000	$ 8,034,000 (FTEs: 91)	$ 8,701,000 (91)	$ 667,000 (—)

Purpose and Method of Operation

This activity provides funds for staff and support costs for the scientific direction, management, administration, coordination, planning and evaluation of the Division and its five extramural research programs. It also provides staff for the Research Centers at Minority Institutions Program which the Division administers for the Office of the Director, NIH. Scientific and administrative staff work together in the planning, development and execution of these programs to provide the research community with the resources essential for the conduct of biomedical research.

Scientific program staff and the grants management staff administer all aspects of the Division's resource center grants, research grants, research training grants, and research and development contracts. They coordinate the peer review of competing applications for scientific merit and program relevance. They also serve in a liaison capacity for applicants, grantees, other components of NIH, the Department and other interested organizations. In addition, they monitor and report scientific and fiscal information relevant to extramural programs.

This activity also provides funds for the operation of the Office of the Director, the Office of Science and Health Reports, the Office of Program Planning and Evaluation, and the Office of Administrative Management, which performs administrative services for the Division such as financial management, personnel management, and data management functions. In addition, this activity provides funds for financing the NIH central services activities including the NIH management fund, the DHHS/NIH general expense fund, and the NIH service and supply fund.

Rationale for the Budget Request

The 1987 budget request for Research Management and Support is $8,701,000, an increase of $667,000 over the comparable 1986 level. This level reflects increases for administrative mandatory costs of $757,000 offset by savings from management improvements and program decreases amounting to $90,000.

During 1987 continued emphasis will be placed on management reforms and improving operating efficiency. The Division will move toward more management improvements including office automation, paper reduction, and streamlined administrative procedures in order to carry out the Division's mission more efficiently.

Research Resources

Detail of Permanent Positions

	1985 Actual	1986 Estimate	1987 Estimate
ES-4..................	3	3	3
Subtotal..........	3	3	3
GS/GM-15..............	6	6	6
GS/GM-14..............	14	14	14
GS/GM-13..............	6	7	7
GS-12..................	9	8	8
GS-11..................	6	7	7
GS-9..................	3	3	3
GS-8..................	1	2	2
GS-7..................	12	11	11
GS-6..................	8	7	7
GS-5..................	3	3	3
GS-4..................	1	1	1
GS-3..................	0	0	0
Subtotal..........	69	69	69
Grades established by Act of July 1, 1944 (42 U.S.C. 207):			
0-6................	7	7	7
Subtotal..........	7	7	7
Total permanent positions.........	79	79	79

TUESDAY, MARCH 18, 1986.

NATIONAL INSTITUTE ON AGING

WITNESSES

DR. T. FRANKLIN WILLIAMS, DIRECTOR, NATIONAL INSTITUTE ON AGING OF THE NATIONAL INSTITUTES OF HEALTH, DEPARTMENT OF HEALTH AND HUMAN RESOURCES

DR. JAMES B. WYNGAARDEN, DIRECTOR, NATIONAL INSTITUTES OF HEALTH

DR. EDWARD L. SCHNEIDER, DEPUTY DIRECTOR, NATIONAL INSTITUTE ON AGING OF THE NATIONAL INSTITUTES OF HEALTH, DEPARTMENT OF HEALTH AND HUMAN RESOURCES

DAVID L. CHICCHIRICHI, EXECUTIVE OFFICER, NATIONAL INSTITUTE ON AGING OF THE NATIONAL INSTITUTES OF HEALTH, DEPARTMENT OF HEALTH AND HUMAN RESOURCES

KARYN S. ROSS, BUDGET OFFICER, NATIONAL INSTITUTE ON AGING OF THE NATIONAL INSTITUTES OF HEALTH, DEPARTMENT OF HEALTH AND HUMAN RESOURCES

DENNIS P. WILLIAMS, ACTING DEPUTY ASSISTANT SECRETARY, BUDGET, DEPARTMENT OF HEALTH AND HUMAN SERVICES

WITNESSES

Chairman NATCHER. This morning we take up the budget request for the fiscal year 1987 for the National Institute on Aging. We have before the Committee Dr. T. Franklin Williams, the Director.

Dr. Williams, before you start with your statement, tell us who you have there at the table with you.

Dr. WILLIAMS. Thank you, Mr. Chairman.

I have Ms. Karyn Ross, our Budget Officer; Dr. Edward Schneider, our Deputy Director; and Mr. David Chicchirichi, our Executive Officer.

Chairman NATCHER. We are delighted to have all of you before the committee. Dr. Williams, we would be glad to hear from you at this time.

Dr. WILLIAMS. Thank you, sir. I have submitted written testimony, which I hope might be included in the record.

Chairman NATCHER. Yes.

Dr. WILLIAMS. I will highlight it here.

Chairman NATCHER. Very well.

THE OLDER POPULATION

Dr. WILLIAMS. I am very pleased to report to you today, at a critically important time in our Nation's research program, as we move towards defining and understanding the aging process and the diseases and disorders of older people, that we have a major challenge in the next 14 years as the number of persons in our country over the age of 85 will more than double.

Many older people are and can be healthy and fully functional, and promotion of these conditions is one of our priorities. On the other hand, we face large increases in the numbers of disabled persons. Unless we can make major advances through research in preventing and treating the chronic problems that disable older people, we face exponential increases in costs.

HIGH PRIORITY RESEARCH

Among these common problems, Alzheimer disease and related dementing conditions are by far the most devastating and contribute the most to burdens on families and to the costs of care. Direct costs are currently estimated to be at least $38 billion per year and are rising rapidly. Research in Alzheimer disease is the highest priority of the National Institute on Aging and accounts for over 25 percent of our total research budget.

Among our epidemiologic studies on older populations, we are finding, Mr. Chairman, that the frequency of dementia may be even higher than we had originally anticipated. In one study, approximately 40 percent of persons over age 85—about double previous figures—are being found to have a significant degree of dementia.

Conversely, in some other areas of the world and other populations, far lower rates are reported. It is clear that we need more careful comparative epidemiologic studies in various populations.

Other research on Alzheimer disease in the past year, using biochemical and molecular genetic techniques, has shown remarkable progress in understanding the nature of the abnormal proteins that occur in the brains of people with this condition. Some of the protein components of the tangles and the amyloid plaques have now been identified, and the genetic basis for the abnormality has been partly identified. We have the opportunity, also, possibly of identifying some of these abnormal proteins in the peripheral blood and in the spinal fluid of victims with the disease. If so, these might serve as the basis for some diagnostic tests for this disease early on.

In another advance reported in the last few months from Baltimore by one of the centers we support, as well as support from other Institutes of the National Institutes of Health, it has been found that another major brain hormone—the so-called Corticotropin Releasing Factor, or CRF—is markedly decreased in certain areas of the brains of Alzheimer victims. The receptors for this CRF, though, are actually increased at the same time, which suggests that suitable replacement therapy—for example, by some compound like CRF—might actually restore some brain function.

In our own Laboratory of Neurosciences in Bethesda, we have some evidence that these changes in the CRF protein can be detected in the spinal fluid, and this offers another possibility for a diagnostic test. There are also very promising opportunities for further genetic studies on Alzheimer disease.

We continue to support and emphasize the need for studies on factors affecting the families and family support systems for victims of this disease.

Other high-priority areas for our research include the other major functional problems that older people commonly have, particularly problems of mobility and urinary incontinence. I summarize some of the evidence about these in my written testimony. Here I would like to mention that there are more than 200,000 hip fractures which occur each year, 80 to 84 percent of these in people over the age of 75. These cost at least $7 billion a year.

We are now encouraging more research on factors involved in falls and in the problem of osteoporosis in the bones, and are working with the National Institute on Arthritis and Musculoskeletal and Skin diseases to increase our joint support for more research on both osteoporosis and osteoarthritis.

In our Baltimore Longitudinal Study on Aging, we are continuing to work towards adding more women volunteers to this fundamental study. We are also proceeding in the development of our new Laboratory of Molecular Genetics.

One of my own personal goals is to increase the numbers of investigators and academic leaders in the fields of aging and geriatrics. We have made some more progress this year by developing several new approaches to achieve this goal.

Mr. Chairman, the NIA considers its mission and efforts to be an investment in the future for all of us. Our FY 1987 budget request is $145,829,000.

I would be very happy to answer questions, sir.

Chairman NATCHER. Thank you, Dr. Williams.

[The statement follows:]

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Statement of the Director
National Institute on Aging

I am pleased to report to you today at a critically important time in our nation's research program aimed at defining and understanding the aging process, the medical and social imperatives of this century. In the next 14 years, the number of persons in our country over age 85 will more than double. Many older people are and can be healthy and fully functional, but unless and until we can make major advances in our prevention and treatment of the chronic problems that are common in older people, we face large increases in number of disabled persons and exponential increases in costs.

To understand aging, scientists must examine an immensely broad range of topics. Molecular biology, immunology, pharmacology, neurology, psychology, social and behavioral sciences, epidemiology, and genetics are but a few of the disciplines that must be part of any comprehensive study of aging.

The ultimate goal of all research on aging is to reduce the impact of age-related disabilities and diseases, thereby improving the quality of life in the later years. This goal does not mean, however, that only those individuals 65 and older will be affected by the results of aging research. To bring about significant improvements in the health of future generations, people of all ages will need to make changes in lifestyle, diet, and personal health care practices. Studies conducted and supported by the NIA will help define these lifestyle changes.

Research on Alzheimer disease, the most common form of dementia among the elderly, continues to be a high priority for the NIA. We know many things about Alzheimer disease that we didn't know a decade ago. More physicians know it when they see it; they even know how to treat some of its less serious symptoms, but they don't know how to stop it from getting worse or how to cure it. Scientists know more about what goes on inside the brains and bodies of people who have it, but they still don't know what causes it. Policymakers know that more people have it, and that the cost of their care could bankrupt a nation in the years to come if nothing is done about it. And the general public knows it exists...which is more than they knew a decade ago.

By most estimates, Alzheimer disease is the cause of serious confusion and forgetfulness in some 2.5 million American adults. This is five times the estimate that appeared in the literature 10 years ago when the NIA began its first studies in this area. But these latest estimates stand for more than just growing numbers of older people. They reflect, in addition, a more sophisticated, if not yet perfected, approach to diagnosis; better training of health care professionals regarding the problems of old age; and a greater awareness of Alzheimer disease and its symptoms among the general public.

In fact, according to experts at Harvard University, our current estimates of the number of Alzheimer victims may still be too conservative. In one of the four NIA supported Established Populations for Epidemiologic Studies of the Elderly, the Boston group has found that more than 10 percent of the study population over age 65 may be suffering from some sort of dementia. This is double the frequently stated estimate of 5 percent. The numbers reach almost 40 percent among those aged 85 and older.

According to the Alzheimer's Disease and Related Disorders Association, $35 billion was spent last year on the care of Alzheimer patients. This includes the costs of nursing home and other long-term medical care, but doesn't begin to account for the emotional and social costs of the disease. In a soon-to-be-published paper, NIA health economist Dr. William Cartwright and colleagues at Howard University and Pennsylvania State University have tallied some of the specific costs of Alzheimer disease, suggesting that $35 billion is just the tip of the iceberg, and speculate that the special services required by dementia victims might cost more than $38 billion, with another $39 billion for indirect costs to the families involved, with a total, minimum, cost of $77 billion.

The NIA supports major research activities on Alzheimer disease and related dementias in older people, including 10 Alzheimer Disease Research Centers. These centers have begun to produce important scientific knowledge. At one of the centers, it has been found that nuclear magnetic resonance (NMR) imaging can detect very early signs of small strokes or multi-infarct dementia and distinguish them from Alzheimer disease. This will enable physicians to institute appropriate treatments, thus preventing further deterioration. Research at other centers is defining the genetic component of Alzheimer disease.

One of the characteristics of Alzheimer disease is the presence of amyloid fiber deposits in the brain's blood vessels. An NIA supported scientist has isolated and analyzed these amyloid fibers of Alzheimer patients and found a unique protein not seen in healthy individuals. Interestingly, the same protein appears in the amyloid deposits of Down syndrome, representing another link between Alzheimer and Down syndrome. Future plans call for the use of monoclonal antibodies to take a closer look at this unique protein with the hope of isolating its precursor. This work reveals yet another clue that Alzheimer disease is a systemic disorder, and may lead to a simple diagnostic test for the disease.

Since the late 1960's, some scientists have speculated that Alzheimer disease might result from a so-called "slow virus" infection, caused by an infectious agent that hides within the body for years before producing devastating disease. In this area, too, our questions have become more sophisticated, with scientists looking at the fundamental processes involved in the development of the virus. Previous studies have identified the infectious "prion" protein associated with some slow-virus disorders. More recently it has been demonstrated that the prion is part of a larger protein present in both normal and infected cells. In normal cells, the larger protein is completely broken down by enzymes; in infected cells, the defective breakdown leaves the prion intact. This prion has a fibrous structure that resembles certain filaments found in the brains of Alzheimer patients.

The primary goal of geriatric research and treatment is to maintain effective functioning and independence in living for older people, to the maximum extent possible, in the face of chronic diseases and disabilities. The extent to which we can improve our capabilities to address such problems successfully will largely determine what the burden of care is going to be for individuals, families and society, as the number of old and very old people rapidly increases. A number of disorders and diseases that afflict older people and result in disability and institutionalization have received too little attention from the medical research community. These include such major functional disabilities as urinary incontinence and problems of mobility with the frequently associated complications of falls and hip fractures. The NIA is developing programs to address these conditions specifically.

Urinary incontinence is a common disorder that affects not only many institutionalized patients, but many community-dwelling men and women as well. Estimates indicate that about half of all nursing home residents and 7 to 14 percent of noninstitutionalized older adults are incontinent of urine.

Intramural scientists at the NIA's Gerontology Research Center (GRC) in Baltimore, Maryland, have just published their very encouraging results of a study of the therapeutic effectiveness of a combination of physical therapies and behavioral training procedures in elderly women affected by either stress incontinence, bladder hyperreflexia, or urge incontinence. They have documented a major reduction or elimination of incontinent episodes in 80 percent of the patients.

Such accomplishments, if they can be achieved more generally, could help considerably to reduce the costs of care for persons with this problem — a cost that is estimated to be at least $1.5 billion for patients in nursing homes alone. Five clinical trials of treatment of urinary incontinence are now in progress at academic centers around the country, jointly funded by NIA and the Division of Nursing Research, HRSA. The Baltimore research team, with partial support from the Health Care Financing Administration, is extending its studies in nursing home patients.

Hip fractures are both more common and more serious in older persons. They are a leading cause of disability in older adults and account for a high percentage of nursing home admissions. Of the more than 200,000 hip fractures each year in the United States, 84 percent occur in persons over age 65 years. One year after a hip fracture, 20 percent of the surviving victims cannot walk. In addition to their direct impact on health and independence, hip fractures have been estimated to cost over $7 billion in 1984 and are certainly higher today. A major area of research interest related to fractures is osteoporosis.

Osteoporosis is a degenerative bone disease affecting as many as 20 million Americans, most of them over 50 years of age. The disease results in brittle, fragile bones, and thus is directly related to fractures. It is estimated that over 90 percent of women have significant osteoporosis by age 85. This problem, little recognized in the past, is like Alzheimer disease, a new silent epidemic. Research findings indicate that this disease may have multiple causes. The NIA is collaborating with the new National Institute of Arthritis and Musculoskeletal Diseases to considerably increase research on the causes and potential treatments for osteoporosis as well as for osteoarthritis, another major cause of loss of mobility in older people. There are promising opportunities for comparative studies with other nations and cultures where osteoporosis, osteoarthritis and Alzheimer disease may be less prevalent than in the United States.

With increasing longevity and growth in absolute numbers of older people, the need for improved health and functioning will become overwhelming before the end of the century. There is a pressing need to discover the mechanisms by which age-related declines may be prevented, reversed or ameliorated. Research supported by the NIA suggests that the productivity of the middle years can be extended and that many disabilities of old age can be prevented, reversed, or postponed, thus improving the quality of life for older people and containing the costs of health care and dependency.

Aspects of lifestyle, in particular nutrition and exercise, are thus commanding a great deal of research attention. At the NIA, research on nutrition is attempting to define the nutritional requirements for good health in the elderly; to determine how dietary deficiencies are associated with depressed immuno-competence, depressed cognitive function, or overt metabolic disease; and to determine how eating behaviors change with aging. Research on exercise physiology examines how physiologic (e.g., pulmonary, cardiovascular, or neuromuscular) adaptation to exercise is altered by aging, and whether regular long-term physical activity can help prevent such age-related disorders as hypertension, maturity onset diabetes mellitus, and osteoporosis.

Special opportunities for deeper understanding of the aging process which currently exist need to be capitalized upon. Techniques are available to probe genetic changes, to distinguish aging processes from disease, and to specify the social conditions influencing the ways people grow old. New methods, data, and concepts are becoming available for forecasting life expectancy as well as active life expectancy. The Baltimore Longitudinal Study of Aging, with its highly characterized population of healthy volunteers, wealth of longitudinal date, and multidisciplinary and multivariate approach, is a unique resource to study human aging. Increased knowledge of how biological, psychological, and social aging processes interact to produce particular strengths and weaknesses in older people will be used to identify appropriate mechanisms for preventing diseases and disabilities and enhancing health and independence.

Recombinant DNA technology, a powerful tool for exploration of gene structure and function, has yielded remarkable information about a large variety of genes. Investigators interested in the biology of aging are now employing this technique in the study of genes related to aging processes. Examples of planned and on-going research include identification and characterization of genes preferentially expressed during senescence; analysis of restriction fragment length polymorphisms to identify fragments of human DNA carrying defective genes (e.g., the gene for familial Alzheimer disease); and examination of the relationship between age and transcription of specific DNA sequences.

The population aged 85 and over has been growing at over three times the rate of the population aged 65 and over, while the population aged 95 and over has been growing at twice the rate of the 85 and over age segment. Members of this age group have very high rates of morbidity and disability and are heavy users of care. Almost 25 percent are institutionalized, and 40 to 45 percent of non-instutionalized people need the help of another person in everyday life. Less is known about this age group than about any other. It is now feasible to develop realistic projections of the future size and composition of the Nation's 85 plus population, including future patterns of mortality, morbidity, disability, and need for care. By enhancing Federal databases, gaps in Federal and International statistics on the oldest old can be filled, thus enhancing our ability to study the special problems and needs of this cohort.

Mr. Chairman, the 1987 budget request for this Institute is $145,829,000. I will be happy to answer any questions.

BIOGRAPHICAL SKETCH
T. Franklin Williams, M.D.
Director, National Institute on Aging

Birthdate: November 26, 1921 - Belmont, North Carolina

Education: B.S., University of North Carolina, 1942; M.A., Columbia University, 1943; M.D., (Cum Laude) Harvard Medical School, 1950

Professional History: 1983 to present, Director, National Institute on Aging, NIH; 1983, J. Lowell Orbison Alumni Distinguished Service Professor; 1982-1983, Director of the Geriatric Unit, Monroe Community Hospital, Rochester, N.Y.; 1980-1983, Co-Director, Center on Aging, University of Rochester Medical Center; 1968-present, Professor of Medicine and of Preventive, Family and Rehabilitation Medicine, University of Rochester; 1968-1982, Professor of Radiation Biology and Biophysics, University of Rochester; 1968-1982, Medical Director, Monroe Community Hospital, Rochester, N.Y.; 1977, L.S. McLeod Visiting Professor of Geriatric Medicine, University of Adelaide and South Australia Postgraduate Medical Education Association; 1956-1968, Instructor to Professor of Medicine and of Preventive Medicine, University of North Carolina; 1954-1956, Fellow in Medicine, University of North Carolina; 1953-1954, Assistant in Medicine, Boston University; 1953-1954, Senior Resident Physician, Boston Veterans Administration Hospital; 1950-1953, Intern and Assistant Resident Physician, John Hopkins Hospital; 1942-1943, Assistant in Chemistry, Columbia University.

Military Service: 1983 to present, Assistant Surgeon General, U.S. Public Health Service; 1943-1946, Communications Officer, U.S. Naval Reserve, active duty.

Societies and Associations: American Association for the Advancement of Science (Fellow); American College of Physicians (Fellow); American Federation for Clinical Research; American Public Health Association (Fellow); American Society of Human Genetics; American Geriatrics Society; American Diabetes Association; Society for Experimental Biology and Medicine Rochester Academy of Medicine; New York and Monroe County Medical Societies; Gerontological Society of America; New York State Public Health Association; Institute of Medicine, National Academy of Sciences; The Royal Society of Medicine; and Academia Medicorum Litteratorum.

Honors and Awards: Phi Beta Kappa; Alpha Omega Alpha; Sigma Xi; Member, Institute of Medicine; Diplomate, American Board of Internal Medicine; Diplomate, National Board of Medical Examiners; Markle Scholar in the Medical Sciences; Special Fellow, Department of Physiology, Vanderbilt University; and Honorary Member, American Academy of Orthopedic Surgeons.

Publications: Author of over 112 scientific papers and abstracts.

CENTER GRANTS

Chairman NATCHER. You are supporting, I believe, 12 research centers, 10 of which are Alzheimer centers. What are the other two centers?

Dr. WILLIAMS. One is a center on overall aging research, a long-standing center in aging research based at Duke University; the other is a data center based at the University of Michigan where we accumulate data from a variety of studies and organize it so that many scientists can use it. It is a data resource center.

Chairman NATCHER. Now, if you will, give us a list of the 12 centers along with the amount of current grants for each.

Dr. WILLIAMS. The fiscal year 1986 funding level for individual centers has not yet been determined, since most are funded late in the fiscal year, I can however give you the recommended funding levels.

Chairman NATCHER. Dr. Williams, if you want to you can put that in the record.

Dr. WILLIAMS. I will provide that information for the record.

Chairman NATCHER. That will be fine.

[Information follows:]

NIA CENTERS

The exact cost per center has not yet been determined for fiscal year 1986. The total estimated full recommended level of $12,301,300 is $2,352,300 below the fiscal year 1986 funds available. This amounts to approximately a 19 percent shortfall. It should be pointed out that in addition to the 12 centers under discussion, the NIA co-funds a General Clinical Research Center and five primate research centers with the NIH Division of Research Resources. These are DRR centers and consequently are not counted in the NIA centers line. However, the NIA funds committed to them are included.

Estimated full recommended levels for NIA Center grants

Alzheimer Disease Research Centers:	
Duke University	$1,090,892
University of California/San Diego	1,077,831
University of Pittsburgh	1,404,219
Harvard University	1,685,946
University of Washington	1,492,504
Mt. Sinai School of Medicine	714,894
University of Southern California	650,566
University of Kentucky	347,719
Johns Hopkins University	1,116,834
Washington University	1,135,818
Other Center Grants:	
Research support services of Gerontology Center, Duke University	267,527
Factors in aging: Developing research resources, University of Michigan/Ann Arbor	458,000
General Clinical Research Center (with DRR)	677,623
Primate Research Centers (with DRR)	180,927
Total, full recommended level	12,301,300

ALZHEIMER DISEASE RESEARCH SUPPORT

Chairman NATCHER. Do you think that support for the Alzheimer centers should be increased if additional funds become available?

Dr. WILLIAMS. We have given a high priority to funding the maximum we can in this very important area. However, we are not funding these centers to the full level approved. From the very beginning, because of the limitations on our centers' funding, we have had to underfund them. Currently, we are funding them at about 80 percent of the approved funding levels. We could justifiably increase the support to these centers for a number of unfunded projects they are already approved to undertake if there were more funds available.

Chairman NATCHER. Do you favor the creation of more Alzheimer centers or would you expand the existing ones first?

Dr. WILLIAMS. I would certainly do the latter, Mr. Chairman. I think that we have these centers well on the way in pursuing very important research and they are approved and ready to expand their efforts in very important ways.

Chairman NATCHER. If you had more money, would you use it to increase support for regular research grants, or would you use it to increase support for Alzheimer centers?

Dr. WILLIAMS. That is a hard question to answer because both are important. I think that if there were money specifically targetted in the Alzheimer's area, I would probably try to bring the centers up to their fully-approved funding and then consider other research grant opportunities, although there are many approved research grant projects that we also are not able to fund in this area.

GRANT REFERRAL GUIDELINES

Chairman NATCHER. How many study sections are reviewing applications for aging research?

Dr. WILLIAMS. We have two special study sections in our own Institute, the Aging Review Committee and the Geriatrics Review Committee, which review program project grants, training and career awards, and center applications. Our regular research project grants go to 20 or 30 of the review committees in the Division of Research Grants, or I am told as many as 50 of those various review committees.

Chairman NATCHER. Since many scientific disciplines are involved in research relating to aging, how is the decision made to refer an application to the Aging Institute for funding rather than some other Institute?

Dr. WILLIAMS. The NIH Division of Research Grants of NIH develops referral guidelines in collaboration with all of the NIH Institutes. We all participate in trying to provide guidelines for just where a given application might be best managed. When we know that certain applications are coming in, we can indicate that we have a special interest or competence in the area of that application. In relation to aging, the guidelines are based around the question of whether aging is one of the important variables in the study. Either the whole study is directed specifically to aging or aging is an important characteristic that the application is considering.

RESEARCH COLLABORATION

Chairman NATCHER. Now, Dr. Williams, to what extent are you collaborating with other Institutes to support specific projects?

Dr. WILLIAMS. Among our well-established areas of support in Alzheimer disease, we have collaborated with the National Institute of Neurological and Communicative Disorders and Stroke, the National Institute of Mental Health, and the National Institute of Allergy and Infectious Diseases in developing our centers. We collaborate with the National Heart, Lung and Blood Institute on an important clinical trial on systolic hypertension in the elderly. We are working with the National Institute on Arthritis and Musculoskeletal and Skin Diseases to develop programs of research on osteoporosis and osteoarthritis. Finally, we support some combined research with the National Cancer Institute.

AGING RESEARCH

Chairman NATCHER. In your statement, you point out that a number of disorders and diseases that afflict older people and result in disability and institutionalization have received too little attention from the medical community.

How much success are we having in getting scientists interested in conducting research relating to the aging?

Dr. WILLIAMS. Fortunately, this interest is growing year by year; I would say almost exponentially. In the most recent survey just completed, of all medical schools—including schools of osteopathy—in this country, 120 out of 135 have geriatric educational program content of one type or another. This is also being reflected more strongly in the interests of faculty, research scientists and teachers in this field. Nonetheless, we still are far short of having the numbers we need, in my judgment, as we have reported to this Committee before.

Chairman NATCHER. What proportion of the research you support would you define as behavioral research?

Dr. WILLIAMS. We have a separate extramural program for behavioral sciences research. That program manages about 21 percent of our research funding. In other words, about a fifth of our research activity is in the behavioral research area and it has been at about that level for the last several years.

GROWING AGING POPULATION

Chairman NATCHER. You pointed out in your statement that in the next 14 years the numbers of persons in our country over age 85 will more than double.

Do you think, Dr. Williams, that as a nation we are prepared to meet the needs of our growing aging population?

Dr. WILLIAMS. Not in the way I think we all want to, Mr. Chairman. In the first place, we don't know as much as we need to know about just what it is like to be in the 85 to 100-year-plus range in which many of us, hopefully most of us, will be living in the not too distant future. A basic need is to have more information about both health and illness in these very late years. Then, based on that, we will I am sure be able to do more in the way of promoting health, maintaining function and managing the chronic problems that do come along.

Chairman NATCHER. Do you think that our Nation's physicians are adequately prepared to deal with the special health problems of the aged?

Dr. WILLIAMS. They really are not. I think that shows up in many ways even though, as I have mentioned, there is increasing interest in both medical schools and in the practicing profession. The number who are capable of teaching and giving leadership in this field is still, by our estimate, only about 10 percent of those needed. In addition, we find in the continuing practice of physicians, many examples of unawareness of what would be good medical practice for older people.

Chairman NATCHER. Are you optimistic, Dr. Williams, that we will find better ways to prevent or treat the special problems of the elderly, such as incontinence, senile dementia, memory loss, broken bones, depression, and so on?

Dr. WILLIAMS. I certainly am. I think we can cite some very promising and satisfying examples just in the last few years. For example, urinary incontinence studies done in our own research laboratories in Baltimore have shown that in approximately 80 percent of women ~~over~~ the age of 60 living in the community, who have this problem, it can be corrected. Other clinical trials that we are supporting are also demonstrating effectiveness in controlling this very common and disabling problem.

I believe that we will certainly make advances in our understanding and management of osteoporosis and the risk of broken bones and the risk of falls and fractures.

In Alzheimer disease, the frontiers are rapidly opening up our understanding of this disease. There is more hope than certainty about when we will have some answers that prevent or cure it, but I don't have any doubt that we will achieve that goal.

ALZHEIMER DISEASE DIAGNOSIS

Chairman NATCHER. What are the accepted criteria for the diagnosis of Alzheimer disease?

Dr. WILLIAMS. Criteria have been developed in some detail in collaboration between our Institute and the National Institute of Neurological and Communicative Disorders and Stroke and the National Institute of Mental Health. These are now published. Basically, the criteria consist of a usually slow, but progressive dementing condition characterized usually, first of all, by some serious memory losses and the absence of other diagnosable and often treatable conditions for dementia.

There are a whole host of problems that can produce mental changes and these have to be carefully looked for before one arrives at the diagnosis of Alzheimer disease. Basically, this diagnosis remains a diagnosis by exclusion of other conditions and is based on its course, but we are getting closer to being able to diagnose it more precisely.

Chairman NATCHER. How do you distinguish, Dr. Williams, Alzheimer disease from other forms of senile dementia?

Dr. WILLIAMS. First of all, the course is a relentlessly progressive disease. Second is the absence of findings that would point to other causes of dementia in old people. For example, the single other most-common cause is our so-called multi-infarct dementia or damage from multiple small strokes affecting the brain. People who have that problem typically have weakness or signs of the other small strokes, and we can usually make that distinction. Then there are a number of other tests we can do to pick up other diagnosable conditions.

Chairman NATCHER. Mr. Roybal, I yield to you.

Mr. ROYBAL. Thank you, Mr. Chairman.

Dr. WILLIAMS. Good morning.

Mr. ROYBAL. Dr. Williams, I have only a few questions, but they also have to do with Alzheimer disease.

Dr. WILLIAMS. Yes, sir.

ALZHEIMER DISEASE RESEARCH CENTERS

Mr. ROYBAL. I am very interested in that. I have seen families with patients in their home and see the tremendous suffering that goes on. So I am interested in what the ten centers are doing.

You told the Chairman that ten centers are funded at an 80 percent level. Does that mean that all ten centers are funded at an 80 percent level?

Dr. WILLIAMS. No, sir. There is some variation in that.

What we did as we made the award was to negotiate with each center based on a delay in starting up different parts of their approved project. The table that Mr. Natcher asked for earlier shows the actual figures for each center. It varies in terms of the percentage from one center to the other.

Mr. ROYBAL. All right. Then all ten centers are not funded at an 80 percent level.

Dr. WILLIAMS. That is correct.

Mr. ROYBAL. There is a variation.

Dr. WILLIAMS. Yes, sir.

Mr. ROYBAL. Now, what unique contributions have the ten Alzheimer centers made to the progress in Alzheimer disease research?

Dr. WILLIAMS. Each one has its own contributions to make. For example, at the Boston Alzheimer Disease Research Center, they have found evidence, using the Nuclear Magnetic Resonance (NMR) approach to examine the brains of Alzheimer victims or presumed Alzheimer victims, in some of small areas that are probably brain infarcts—small brain strokes—that had not been recognized by any previous technique. They are pursuing the important role of the NMR in understanding and helping diagnose the Alzheimer patient.

At the center at the University of Southern California in Los Angeles, the group there has a very good base for studing autopsies on Alzheimer victims. They are pursuing very active studies on the pathology of this condition. There is also a very active program on the pathology in the brain in Boston and in Pittsburgh.

The University of Washington Center in Seattle, is one of the leading places doing research on the genetics of Alzheimer disease. They have good information on families who appear to have the dominant form of this disease, not the common form but a definitely identified form, and they are doing some very exciting work on the genetics of Alzheimer disease. Again, a couple of the other centers are working on that same subject.

I have already referred to the work they are doing at Johns Hopkins on the Cortotropin Releasing Hormone they have just identified in the brains of Alzheimer victims.

FAMILY STRESS

Mr. **Roybal.** Dr. Williams, I think that what the centers are doing is most commendable. However, we have not progressed far enough yet to be able to take out information and use it in the local community: that is, directly with the family.

Is there anything that a family can do besides suffer?

Dr. **Williams.** Yes, there is. One of NIA's areas of research support is trying to understand better what works—what is most useful in terms of family support approaches. That includes trying to understand the dynamics within the family—how different types of families with different backgrounds interrelate with and support the Alzheimer patients. It is clear that family support groups and day programs and respite care arrangements can make a lot of difference in the quality of life of the family members and make a difference in the degree to which they can continue to care for their family members.

FAMILY SUPPORT SERVICES

Mr. **Roybal.** But that function is not being done by any of the ten Alzheimer centers. Is that correct?

Dr. **Williams.** A few of them have some research projects on family support.

Mr. **Roybal.** I am talking about direct involvement with the family, with the community in the process of taking care of patients with Alzheimer disease.

Dr. **Williams.** Our involvement in those activities is very limited. The centers provide a diagnostic service where they try to identify patients with this disease, and they do provide dissemination of information. One of the requirements for the centers was that they be a source of dissemination of information about Alzheimer to the public and to professionals. Each of these centers has an educational program; but they do not provide direct services to the families.

Mr. **Roybal.** Now, don't you think that direct services to the family would be something that would be most desirable and very badly needed?

Dr. **Williams.** Yes, sir. It certainly is.

Mr. **Roybal.** Is there any prospect that in the future something like that can be done?

Dr. **Williams.** I believe it can be done and I think that these centers would serve as a suitable focus for that. This is currently outside the research and training mission of the NIA. But I think it is a type of thing that a center could well attempt to serve as a focus for doing.

Mr. **Roybal.** But it is closely enough related so that it can be done and that funding for that center could be used for that purpose.

Dr. **Williams.** Yes, sir, under suitable guidelines and policies.

Mr. Roybal. I would like to see something like that. I have not seen anyplace that I go any help coming. You know as well as I do that most of the time it is a woman that is taking care of either an elderly mother or father; that they are practically slaves to that particular patient on a 24 hour basis, no rest.

I have one particular friend that I would just like to tell you about very briefly who is taking care of her elderly parent. The wife who takes care of the parent looks almost as old as the parent.

Dr. Williams. Because of the care burden.

Mr. Roybal. The person is completely worn out with absolutely no help at all. As I go throughout my district, I see that same scene duplicated over and over and over again; and they ask me, is there anything that we can do? Where can we go to get some help?

I don't have any place to recommend them to.

Dr. Williams. Fortunately, services for victims of Alzheimer disease are growing up all over the country, not just in our centers but through hospitals and clinics. I believe that we need to try to provide more services as a national goal.

RESEARCH COORDINATION

Mr. Roybal. Thank you. One last question, Dr. Williams.

It is my understanding that NIMH and the Administration on Aging are also conducting research on the chronic-care needs of persons with Alzheimer and other disorders.

To what extent is the work of NIA coordinated with these other agencies?

Dr. Williams. In the local setting, wherever we have some research going on—like our centers, for example—I know there is a local working relationship wherever there happens to be two or three sources of funds that relate to the same area, like Alzheimer disease. That applies to our collaborative support of research with several of the other Institutes. I know from personal experience that the directors of these different programs, of the type you mentioned, try to collaborate at the local level.

Mr. Roybal. Is there a specific program or a specific place or a city that you can cite as an example of the program that is good?

Dr. Williams. I know that some of these programs are shared in Buffalo and in Rochester. Some of my own background experience is in that part of the country.

Mr. Roybal. Do you know of any in Los Angeles or anywhere in California?

Dr. Williams. I am not certain at this moment, sir.

Mr. Roybal. I would appreciate it if you would give me some information on that.

Dr. Williams. We certainly will.

Mr. Roybal. We would like to see if we have anything in Los Angeles that may resemble the type of program we are talking about.

Dr. Williams. We will certainly provide that, sir.

Mr. Roybal. Thank you, sir.

[Information follows:]

RESEARCH COLLABORATION IN CALIFORNIA

The National Institute on Aging is involved in a number of collaborative research programs in California. One research project on enhancing caregivers' capacity to care for frail older people is being conudcted at the Geriatric Research, Education and Clinical Center (GRECC) of the Veterans Administration Medical Center in Palo Alto. The research is supported with NIA funds, while staff salaries are paid by the Veterans Administration.

The NIA Teaching Nursing Home has been designed to encourage collaborative efforts between academic medical centers and nursing on health problems in older persons. The Teaching Nursing Home at Stanford University includes as its major components: the Veterans Administration Nursing Home Care Unit at the Menlo Park division of the Palo Alto VA Medical Center, a 150-bed facility delivering intermediate care and skilled nursing care; Lytton Gardens, a recently opened facility for older people with independent living and skilled nursing care; the Masonic Home, a skilled nursing care facility and residential living unit; and finally, the Mid-Peninsula Health Service, a consumer-owned, fee-for-service health care service with comprehensive out-patient primary care and home health services.

There are also great expectations for collaboration for the Alzheimer Disease Research Centers (ADRCs). The ADRCs conduct basic, clinical and behavioral research on Alzheimer disease and train scientists and health care providers. In addition, one of their most important duties is to serve as a vital link between investigators from the various disciplines studying dementia, and as a link between those investigators and health care professionals and voluntary support groups in the community. There are two ADRCs in California, one at the University of California/San Diego and one at the University of Southern California in Los Angeles. Both are already involved in the types of collaboration just described.

Dr. Zaven Khachaturian, Chief of the NIA Physiology of Aging Branch within the extramural Biomedical Research and Clincial Medicine Program, is currently serving as a resource person to the State of California Alzheimer Disease Taskforce.

The Alzheimer's Disease and Related Disorders Association (ADRDA) is one of the best sources of general information on long-term care programs. The various chapters of the ADRDA serve as information clearinghouses for miscellaneous services and activities available to Alzheimer patients and their families in any given area. In the State of California, there are 13 ADRDA chapters and affiliates which link Alzheimer families to services in the community. The Los Angeles chapter (Contact: Stephany Gore at (213)-473-1446) and the San Diego Chapter (Contact: Jay Glenner at (619)-453-9616) have developed or are in the process of planing some extremely innovative long-term care services for Alzheimer patients.

ALZHEIMER DISEASE RESEARCH

Mr. CONTE. Dr. Williams, we are very pleased to have you back before our Subcommittee.

Dr. WILLIAMS. Thank you, sir.

Mr. CONTE. As one of the sponsors of a recent Office of Technology Assessment Workshop on Alzheimer disease, I want to thank you for your participation and thoughtful contribution to that seminar. As that seminar illustrated, Alzheimer is a far-reaching disease, one which we are only scratching the surface of at this time.

Dr. WILLIAMS. Yes, sir.

Mr. CONTE. My hope is that by bringing experts together, we can concentrate our knowledge on this disease, get the public more concerned and aware, and initiate a real push to solve the devastation Alzheimer disease is causing in this country of ours.

According to your justifications, Doctor, you propose a rescission for 1986, all of which comes out of new research project grants. Of the 24 projects you are slated to lose, do you know how many are directly related to Alzheimer disease?

Dr. WILLIAMS. That would depend on how we would be best able to handle this reduction. We give a high priority to the Alzheimer disease area, our highest priority, and we would try to minimize the impact on this particular area. It is hard to give a precise figure, but I think we would almost certainly have to reduce by several the awards we would make in the Alzheimer field given the fact that we have other priorities and we try to look at scientific merit as one of our most important considerations.

Mr. Conte. Let me ask you this, then. In the revised 1986 budget request, what amount of research dollars will be focused on Alzheimer, and how does that compare to FY 1985? Can you tell us that?

Dr. Williams. Yes, sir. I think that our figures for our Institute for 1986 are $32 million whereas, in fiscal 1985, we expended $28.8 million for Alzheimer disease.

Mr. Conte. Can you give me the same estimates of the budget requests in FY 1987?

Dr. Williams. The budget request in 1987 is $32 million, again.

Mr. Conte. $32 million.

Dr. Williams. Yes.

INCREASE IN APPLICATIONS

Mr. Conte. Doctor, in recent years has there been an increase in the number of researchers applying for project grants to study aspects of Alzheimer disease?

Dr. Williams. Yes. There has been. I could give you some precise figures on that.

Mr. Conte. If you please.

Dr. Williams. We have had a rapid growth in the numbers of these.

Mr. Conte. OK. Put some precise figures in the record then, please.

Dr. Williams. Certainly.

[Information follows:]

Alzheimer Disease Applications

In fiscal year 1980, the National Institute on Aging received 81 applications in the areas of neurosciences and cognitive biopsychology and aging. Approximately 30 percent—or 24 applications—were directly or indirectly related to Alzheimer disease. In fiscal year 1985, 263 applications were received of which about 75 percent—or 197 applications—were related to Alzheimer disease. This is nearly an 8 fold increase.

ALZHEIMER DISEASE RESEARCH CENTERS

Mr. Conte. As you know, this Subcommittee established five Alzheimer research centers in 1984 and another five in 1985. What affect will the Gramm-Rudman-Hollings sequester have on these centers? And what will be the effect of the further reductions proposed in 1986?

Dr. Williams. The answer to that is somewhat complicated.

Mr. Conte. OK. Go ahead.

Dr. Williams. The initial funding for each of these two sets of centers was not sufficient to permit us to fund fully the approved projects in them. So from the very beginning we have had to negotiate down from the full recommended level and delay the start-up of some of the projects. We actually were about $1.6 million underfunded already for the approved projects in these ten centers at the fiscal year 1986 Appropriation level. The sequestration law reduced that by another $500,000 so that now we are about $2.1 million underfunded in fiscal year 1986. In other words, that added about another 25 percent to our underfunding.

Mr. CONTE. Right.

According to your statement, the costs of caring for Alzheimer patients runs about $77 billion annually. It would seem to me that we should be increasing the potential of these centers, particularly in the area of health service research. Do you think the work of these centers could be effectively expanded, say by adding a health service research component to the clinical and biomedical mandates they already have?

Dr. WILLIAMS. I think that there would be steps that could be and should be taken in this direction. In our own Institute's activities, we don't ordinarily support health services research. We support clinical trials and we support evaluative research. We are not really constituted to fund or manage large new service programs, but we are capable of carrying out evaluative research on new programs.

Mr. CONTE. Tell me, Dr. Williams, how much money do we need to add to the centers' budget just to maintain the current services in 1987?

Dr. WILLIAMS. For the centers' budget.

Mr. CONTE. Yes.

Dr. WILLIAMS. It would be $2.3 million.

Mr. CONTE. We need $2.3 million more.

Dr. WILLIAMS. Yes, sir.

Mr. CONTE. From 1985?

Dr. WILLIAMS. From 1985. Actually for the 1985, that is correct.

Mr. CONTE. No, no. For 1987.

Dr. WILLIAMS. For 1987.

Mr. CONTE. Just to maintain the services we had in 1985.

Dr. WILLIAMS. Just to maintain it would be about $2.3 million more.

Mr. CONTE. OK.

Dr. WILLIAMS. That is over 1986.

Mr. CONTE. Right.

Do you have any estimates what it would cost to get them involved in some kind of health service research as well?

Dr. WILLIAMS. I'm sorry, I do not.

ALZHEIMER DISEASE REGISTRY

Mr. CONTE. OK.

In last year's bill, we agreed to add $2.5 million to your budget for the development of an Alzheimer Registry. Has that money been awarded yet?

Dr. WILLIAMS. No, sir. We are issuing a request for applications right now and we expect to make the award in this fiscal year. We anticipate 10 to 20 applications and we will award either one or a very few such registries.

Mr. CONTE. Tell us, Doctor, what benefit will we get from this kind of registry?

Dr. **Williams.** I think this type of registry will serve a very important need, namely, it will allow us to pull together information on proved cases of Alzheimer disease, well established using standard definitions and diagnostic criteria, which can then serve as a basis for shared research efforts among different centers and settings. It also eventually can serve as a basis for identifying patients who would be potential candidates for clinical trials. That is one major area. We also envisage that such a case registry would undertake some more epidemiologic studies on the distribution of this condition in selected populations.

Mr. **Conte.** That is quite a task. Do you think $2.5 million will cover it?

Dr. **Williams.** Frankly, no. I think this will get us started and we will have to see where it goes from there.

GERIATRICS AND GERONTOLOGY

Mr. **Conte.** Doctor, I am particularly concerned that whatever advances we are making in terms of diagnosis and treatment of Alzheimer are getting out into the field. Many of our senior citizens prefer to stay with their long-time doctors that they have been going to for years, rather than seeking out the newest specialists in this field. What are we, or should we be doing to make sure that doctors in the field have the best and the newest information with regard to Alzheimer disease?

Dr. **Williams.** This is certainly important because the bulk of care is going to be provided by the primary physicians for Alzheimer victims as well as other problems in older people. One of our aims, certainly, is to help disseminate knowledge to all practitioners.

We do this in several ways. All of our centers are required to have a dissemination program for professionals as well as the public on the latest knowledge about Alzheimer disease. Our public information office puts out regular progress reports that are very widely distributed to the profession as well as the public and we have articles supported by our Institute—the research outcomes and review articles—constantly in medical journals.

TRAINING

Mr. **Conte.** Dr. Williams, your justifications claim that training is one of the Institute's highest priorities; but looking at the actual numbers, you are proposing a decrease in training positions from 230 to 190.

With the dramatic increase in the number of older Americans and their heavy use of our health care system, would you not prefer to see an increase in the number of trainees rather than a decrease?

Dr. **Williams.** If funds permitted, yes, sir.

Mr. **Conte.** How do you go about estimating the need for well-trained doctors and scientists in the fields of geriatrics and gerontology?

Dr. **Williams.** Two years ago at the request of this Committee, we led a DHHS Taskforce which made a careful review of the situation in terms of training needs for geriatrics and gerontology. A report based on considerable help from experts in the field as well as from many of the Federal agencies was submitted in fiscal year 1984. There was a clear consensus that we needed a core of faculty in every major teaching institution to help see that essentially all of our future practitioners know enough about aging and the problems of older people to be effective practitioners with older people, which will constitute the majority of all medical practice.

The NIA is attempting to increase training efforts to help provide, first of all, the academic leaders—the teachers and investigators—who then will impart the knowledge throughout the medical curriculum. It is a step-by-step process.

Mr. CONTE. Thank you, Doctor.

Thank you, Mr. Chairman.

Chairman NATCHER. Mr. Stokes.

MINORITY HEALTH

Mr. STOKES. Thank you, Mr. Chairman.

Dr. Williams, your Institute currently has underway a large-scale study on the health of aging black Americans. Can you tell us the current status of that study?

Dr. WILLIAMS. A little over a year ago, we began an epidemiologic study in the Durham County area of North Carolina. It is a population study of predominantly black Americans, and will be an ongoing longitudinal study of essentially every person in that area over the age of 65. We will follow these people over time to determine the general characteristics of the population, their functional status, and the common diseases and disorders that they acquire. This is in parallel with three other similar studies that we have previously started in Boston, New Haven and rural Iowa. The New Haven study, of that group of three, also has a significant minority population in it, but the one in rural North Carolina is predominantly black by choice.

I believe we will learn from this a great deal that we have not had a chance to know before about the life course of older black Americans.

Mr. STOKES. When do you anticipate the completion of this study, Doctor?

Dr. WILLIAMS. The contract for this study is extended for five years. It began in 1985 so it goes through 1990.

FINANCIAL STATUS OF BLACKS

Mr. STOKES. Your budget justification included the following statement: "Research indicated that for nearly one-third of black elderly Social Security and SSI payments are the sole means of support. Contrary to expectations, the more advantaged black elderly—those of higher incomes and education at younger age—receive more social supports than those whose needs are objectively greater."

Could you elaborate on that statement for us?

Dr. WILLIAMS. This is a matter of some data findings. I can only speculate that in many instances more deprived people are not aware of the opportunities that might exist—and quite appropriately—for services that they might receive; and the services often are not as well-developed in more deprived areas, in poorer areas of the country, compared to the services that have been established in more affluent areas.

ALZHEIMER DISEASE

Mr. STOKES. How many Americans have Alzheimer disease?

Dr. WILLIAMS. The current figures are in the range of 2.5 to 3 million, but it is going up all the time. As I mentioned briefly earlier, in one of the recent population studies we have done, the prevalence of Alzheimer disease—or dementia that included Alzheimer disease as the main type—was much higher in the age 85-plus population than in some previous studies. Whether this represents something special about that particular group or whether it is because we did a more careful job of finding everybody is not quite clear; but in that particular study almost 40 percent of the people over the age of 85 had significant dementia.

Mr. STOKES. Are certain groups of people more likely than others to develop Alzheimer disease?

Dr. WILLIAMS. We don't have much evidence about that. There is not much evidence for a difference in sex, for example. There is a little suggestion of more among women, but that may simply be because more women survive into late years.

We do find from reports in the other parts of the world a lower incidence of Alzheimer disease, lower prevalence, than we have generally found in this country. For example, Japan reports a lower prevalence, some areas of the United Kingdom do, and possibly some areas of Nigeria. What we need to do around all these issues is to have more comparable studies to try to see if the differences are real and if they are clues that would explain the differences.

Mr. STOKES. Do we have any studies or do we know whether there is any greater incidence of Alzheimer among blacks and minorities?

Dr. WILLIAMS. The evidence thus far is that there is no difference, but we could use more data.

ALZHEIMER DISEASE RESEARCH SUPPORT

Mr. STOKES. Are we spending adequate resources on this disease?

Dr. WILLIAMS. This is a matter of judgment. We try to give this condition the highest priority among our research topics in our Institute. Overall, our country is spending a little over a tenth of a percent on research in this field compared to the annual cost of the disease. In my own judgment, that is a very small investment in research compared to what the cost is.

Mr. STOKES. Please provide for the record the amount spent on Alzheimer disease by your Institute for 1985 and the amounts estimated for 1986 and 1987.

Dr. WILLIAMS. Yes, sir.

[Information follows:]

ALZHEIMER DISEASE RESEARCH

In fiscal year 1985, the National Institute on Aging spent $28,830,000 for research on Alzheimer disease. Estimates at the fiscal year 1986 Appropriation level and the sequestration level are $34,048,000 and $32,691,000 respectively. We would expect to fund approximately $32,094,000 in Alzheimer disease research at both the fiscal year 1986 revised level and at the fiscal year 1987 President's budget level.

ALZHEIMER DISEASE RESEARCH CENTERS

Mr. STOKES. How many Alzheimer research centers now exist?

Dr. WILLIAMS. There are ten funded centers.

Mr. STOKES. What will be their status under the revised 1986 and 1987 budgets?

Dr. WILLIAMS. These centers have been underfunded from the beginning. We have awarded five each of the last two years as directed by Congress and with all the funds made available. The funds available were not sufficient to provide support at the fully-approved level so that we have negotiated with them to delay the start-up of some of their projects. This continues to be true. As I have mentioned, overall this year, given the sequestration cuts as well as previous underfunding, we are underfunding them by about $2.1 to $2.3 million.

TRAINING MINORITY INVESTIGATORS

Mr. STOKES. Doctor, last year I asked about the summer training program for minority faculty, a new initiative which was being developed. What is the current status of this initiative? Can you tell us what, if anything, has been accomplished?

Dr. WILLIAMS. Let me ask Dr. Schneider to mention a seminar plan that we have for this year.

Mr. STOKES. Dr. Schneider.

Dr. SCHNEIDER. As far as the specific initiative of the summer program goes, that is still in development and we are, again, looking for candidates. The problem is offsetting the cost of bringing those candidates to the NIH.

We are also conducting a conference on Black Aging which will be held in September and which will bring representatives who have studied the social, behavioral and environmental aspects of aging in black populations to Bethesda to exchange their ideas and help to develop new initiatives in this area.

Mr. STOKES. How many research trainees will be supported under your budget in 1986 and 1987?

Dr. WILLIAMS. In 1986, in terms of new ones, it will be 35; and in fiscal 1987, it will be 41 new trainees.

Mr. STOKES. Now, are you doing anything to increase the number of minorities supported through institutional training grants that go to non-minority institutions?

Dr. WILLIAMS. We have encouraged this as a consideration. We don't have a specific requirement or any special allocation of numbers.

Dr. SCHNEIDER. We have made specific trips, though—for example to Drew, to Morehouse, to Howard University—trying to encourage applications and making sure that they are aware of our various training programs.

Mr. STOKES. Thank you very much.

ALZHEIMER DISEASE

Thank you, Mr. Chairman.

Chairman NATCHER. Now, Dr. Williams, your statement tells us that by most estimates Alzheimer disease is the cause of serious confusion and forgetfulness in some 2.5 million American adults. This is five times the estimate that appeared in the literature about ten years ago.

To what extent is this increase simply the result of a change in the definition of Alzheimer disease?

Dr. WILLIAMS. I don't think the basic definition has changed, but what has happened during this period is that far more scientists and clinicians, and the public, are aware of this condition as a disease and not a simple consequence of ordinary aging. When people become demented, we have been much more vigorous in looking for a diagnosis and pinning it down.

So I believe it is more awareness and more effort in diagnosing it rather than a change in definition.

Chairman NATCHER. What do we know about the genetic component of Alzheimer disease?

Dr. WILLIAMS. This is a very challenging issue. We have learned from some of the earlier studies over the last few years that there are limited numbers of families who have a highly inherited form of the disease. It appears to be an autosomal dominant inheritance, a clearcut inheritance.

However, in most instances it does not seem to be that clear. We have begun to get some clues about how to pin down the genetic component of this disease. Dr. Schneider has just told me, today literally, of some new developments. I would like to have him comment on some discussions that he had about the genetics of the disease.

Chairman NATCHER. All right.

Dr. SCHNEIDER. I think what we are looking towards is to identify the location of the gene for Alzheimer disease in those families where it is inherited strongly in a familial way.

Right now, there are some efforts going on, actually in France and also in the United States, to use specific types of genetic markers to, in fact, identify markers all along the human genome. We think we could use the same exact techniques to identify the location of Alzheimer disease in those forms that are highly inherited.

This would be the first step towards isolating that gene, characterizing the gene and seeing how the abnormal gene acts differently from the normal gene giving us one strong step towards understanding the etiology of Alzheimer disease.

INTERNATIONAL RESEARCH

Chairman NATCHER. Dr. Williams, in your statement you mentioned comparative studies with other nations in regard to certain diseases—long words that I am not going to pronounce, Dr. Williams—and in regard to Alzheimer disease.

What do we have here, Doctor?

Dr. WILLIAMS. We have a very fine opportunity to learn more about Alzheimer disease as well as some of the others. Just to note, the others are osteoporosis, thinning of the bones in particular, where there are good clues for major differences in different ethnic groups around the world where the occurrence of these diseases seems to be much less in several instances than in the United States. If this could be established through more comparative studies, then we would certainly be looking for explanations as to why some populations get the disease and others don't. Are there environmental factors that are different that may give a clue to cause, or are there genetic factors that distinguish these different populations? We have some promising opportunities to learn more about these common diseases in older people through comparative studies.

ETHNIC STUDIES

Chairman NATCHER. What can you tell us about the comparative incidence of these diseases among various ethnic groups in the United States?

Dr. WILLIAMS. As far as we know at present, for Alzheimer disease we have not discovered any difference in the occurrence. Osteoporosis, on the other hand, is far less common in black Americans than it is in caucasians. This has been known for some time. This means that there are fewer hip fractures in black Americans. It is an important distinction that we need to know more about.

LIFESTYLE AND HEALTH

Chairman NATCHER. In your statement to the Committee, you say that "Certain aspects of lifestyle, in particular nutrition and exercise, are commanding a great deal of research attention."

What can you report to us about the results of such research at this time?

Dr. WILLIAMS. In my view, some of the most interesting work in the last couple of years has been on exercise where some very careful studies have shown that if people maintained their level of exercise or returned to it—even if they have been sedentary for a while—in their older years, they can achieve virtually the same levels of performance as younger people if they are fortunate enough not to have any chronic diseases. That is, people who are reasonably healthy, if they choose a vigorous lifestyle, can expect to maintain a high level of performance. This relates to research on the muscular system and the skeletal system and the neurological system as well as just general overall observations.

Mr. CONTE. Mr. Chairman, would you yield on that previous question you asked?

Chairman NATCHER. Yes, I will. Go right ahead.

PREVALENCE OF ALZHEIMER DISEASE

Mr. CONTE. I don't recall how you phrased it: comparing the incidence of disease among ethnic groups.

Dr. WILLIAMS. Right.

Mr. CONTE. I thought we had some testimony here, this week that Alzheimer's was predominant in Italy. In fact, one of the Institutes, Dr. Wyngaarden was telling us, was conducting a study in

Boston because of the high incidence of Alzheimer's in East Boston, which is predominantly Italian.

Dr. **Williams**. That has come from our own——

Mr. **Conte**. Was it you?

Dr. **Williams**. That is an established NIA study and is one of the areas where we found a high prevalence of Alzheimer dementia. There are a number of questions to raise about how to interpret it, but the prevalence or frequency of it does seem to be considerably higher there than we have seen in many other places.

Mr. **Conte**. Thank you, Mr. Chairman.

DIFFERENTIAL AGING

Chairman **Natcher**. Yes.

We have all observed that some people, Dr. Williams, seem to suffer from the disabilities of old age much earlier than others.

To what extent would you attribute such differences among individuals to heredity?

Dr. **Williams**. That is something that we really don't have very good experimental information on. We know from life studies that longevity does seem to run in families, but how much is due to what factors is not clear. What we can identify as inherited factors have to do with a number of the disease conditions that many older people do acquire, like atherosclerosis, and vascular diseases.

Dr. Schneider, do you have a comment about this effort?

Dr. **Schneider**. We do have some interesting clues in relation to the aging of the immune system, the system that is very important in dealing with infections. It turns out from work at our Intramural Research Laboratory by Dr. Adler that a certain genetic predisposition related to a certain HLA hapletype can pick out certain individuals whose decline in immune system is much more precipitous with age. That is something we are trying to investigate.

1987 RESEARCH BUDGET

Chairman **Natcher**. Now, you have outlined for us a very ambitious and challenging research agenda.

To what extent, Dr. Williams, does your 1987 budget permit you to pursue this agenda?

Dr. **Williams**. We can certainly pursue a number of aspects and we have tried to. We have to make priority choices. There are some areas in which we have chosen to minimize our encouragement for research because neither this nor any budget will pay for all the possibilities. In terms of the extent to which this budget will support our research I would have to say that we could well go at least twice as far as we are now going in the range of high-quality approved research projects. I have mentioned the underfunding in our centers and in all of our mechanisms.

AWARD RATES

Chairman **Natcher**. What is your award rate for research project applications for 1987?

Dr. **Williams**. Our estimated award rate will be about 25 percent.

Chairman NATCHER. What would you consider to be an appropriate and desirable award rate?

Dr. WILLIAMS. I would judge, based on the quality of the applications we receive and the priority scores they receive, about 50 percent would be a very appropriate award rate.

Chairman NATCHER. How would your award rate for 1987 be affected if, number one, the proposed 1986 rescission of $2,679,000 is not approved; and, number two, the proposal to limit indirect cost is not approved?

Assuming that neither are approved.

Dr. WILLIAMS. That would make our award rate about 20 percent.

DOWNWARD NEGOTIATIONS

Chairman NATCHER. To what extent will you be required to reduce study section approved accounts for competing and noncompeting grants in 1987, Doctor?

Dr. WILLIAMS. It will be in the 8 to 10 percent range of downward negotiations. In other words, we will be able to fund about 90 to 92 percent of the approved funding levels.

Chairman NATCHER. Do you agree with other Institute directors who have told us that negotiated reductions should not exceed 10 percent?

Dr. WILLIAMS. Yes, sir. I would.

Chairman NATCHER. Mr. Roybal, I yield to you.

TRAINING NEEDS

Mr. ROYBAL. Thank you, Mr. Chairman.

Dr. Williams, I would like to ask you to give us a description of what is meant by funding for geriatric training. What does that mean?

Dr. WILLIAMS. What we think of there, in terms of our Institute's mission, is the training of academic leaders: scientists, investigators, members of faculties who are going to be the investigators and teachers in this field.

Now, geriatric training goes beyond what we do. The Health Resources and Services Administration supports curriculum grants and support for individual professional groups; and other agencies of the Federal Government do, also. Most particularly, the Veterans' Administration has a very active geriatric fellowship program. So there are a number of other agencies that are also helping to support geriatric training.

In its broadest sense what we are talking about for geriatric training, in my view, is to prepare all professionals—not just physicians, but all health and social services professionals—for their proper role in the care of older people, and it should be an element in all training: Then, in addition, we need specialized training of the type our Institute tries to support for preparing the teachers and investigators.

Mr. ROYBAL. That would include, then, the training of social workers, health educators, nurses and people that actually deal directly with the general public. Is that correct?

Dr. WILLIAMS. Yes, sir.

Mr. **Roybal**. But that is not being done at the present, is it?

Dr. **Williams**. There is some of that going on through various Government-supported funds as well as local activities. Certainly, there is some of it being incorporated into essentially all curricula of the appropriate schools. But, again in our study for your Committee, we found that in all of these professions there were only 10 to 15 percent of the numbers of faculty needed to do the teaching.

Mr. **Roybal**. In other words, one of the problems that we have is that you don't have enough faculty to do the teaching.

Dr. **Williams**. Yes, sir.

Mr. **Roybal**. But what about the other way? Are there enough social workers and health educators and people that are not doctors involved in the overall health field that would be interested in this?

Dr. **Williams**. There are not enough to provide the range of services needed and there are not enough who are well-prepared. As far as I am concerned it should be a national goal to have more well-prepared people in all of these fields.

Mr. **Roybal**. You do agree, then, that it should be a national goal that we should prepare these people for that.

Dr. **Williams**. Yes, sir. The departmental report to Congress stated exactly that.

TRAINEE LEVELS

Mr. **Roybal**. Now, with regard to your funding for the geriatric training, what activities have been carried out through the training mechanism and how many new training awards were funded in 1985 and are planned for 1986 and 1987?

Dr. **Williams**. In 1985, we had some increase in our funding availability from Congress for both training and career awards. In the training area, specifically, we were able to make 77 new trainee awards in FY 1985 through several different mechanisms to encourage and bring more people into the field. In addition, we had about 20 or so fellows in our own intramural program.

Now, in fiscal 1986 the new awards will be reduced to 35 rather than 77 and in fiscal 1987 it will be 41 compared to 35 new awards. So in each of these two years we are able to support approximately half the number of new trainees as in fiscal 1985.

We have also had to reduce the numbers of intramural fellow positions as a part of our reductions in full-time equivalents.

Mr. **Roybal**. But in the 77 and the 20 fellows, we are talking about the training of medical personnel.

Dr. **Williams**. Yes, sir.

Mr. **Roybal**. Not the health workers.

Dr. **Williams**. Not the other disciplines. That is correct.

Mr. **Roybal**. So we still have somewhat neglected, then, the other disciplines.

Dr. **Williams**. Our Institute has not been involved in training others. That is correct.

Mr. **Roybal**. I understand.

Now, what level of funding would be required to bring the number of new training awards back to the 1986 enacted level?

Dr. **Williams**. To the 1986 enacted level, it would be about $500,000.

Mr. **Roybal**. That is not too much to ask, is it?

Dr. **Williams**. No, sir.

Mr. **Roybal**. Now, if you had the additional funding, do you have flexibility to make the awards? For example, would any restriction on training slots restrict your ability to make the awards?

Dr. **Williams**. We are certainly capable of making them, I think, within the range of numbers available to NIH.

Mr. **Roybal**. So if this money were made available, you could make the awards.

Dr. **Williams**. Yes, sir.

Mr. **Roybal**. I hope you are challenging the Committee.

Dr. **Williams**. Yes.

NEW RESEARCH GRANTS

Mr. **Roybal**. Now, with regard to the funding of new grants—I am just going to have a general question on this—how many new grants are you planning to fund in 1987 and how does that number compare to 1985 and 1986, that is before and after Gramm-Rudman?

Dr. **Williams**. Yes, sir.

Our number planned for fiscal 1987 is 145 new grants. In 1985, we funded 209. In fiscal 1986, our plan was to fund 201. That would have been true with the Gramm-Rudman sequestration act as well. We would have reduced it with the rescission to 177.

Mr. **Roybal**. Well, I can see where we are going backward instead of forward.

Now, how much would be required to fund the number of new grants back up to the 1986 enacted level?

Dr. **Williams**. It would take about $10 million.

Mr. **Roybal**. Now, that is a little bit harder to accomplish, but nevertheless it is a goal that we should be pursuing.

Thank you, Doctor.

Dr. **Williams**. Thank you, Mr. Roybal.

Chairman **Natcher**. Mr. Conte.

TEACHING NURSING HOMES

Mr. **Conte**. Doctor, I believe you are interested in the idea of "teaching" nursing homes, along the same lines as our present academic medical centers, to help increase the standard of care for senior citizens. Tell us a little bit of what you are doing in this particular area.

Dr. **Williams**. Yes, sir. We have made seven awards of the teaching-nursing home type. These are program project grants that are directed at research that concerns issues that affect patients in nursing homes and similar older people, frail and disabled older people.

These awards have required that there be a nursing home environment where research could go on. It is required that there be some involvement of a school of nursing as well as an academic medical center.

The types of projects that I could cite, just for a few examples, include studies on falls in older people and the risk factors that produce falls, musculoskeletal disorders of various types which contribute to frailty and weakness, urinary incontinence studies and other common problems that afflict this particular population.

GENETIC MARKER FOR AGING

Mr. **Conte**. What does the latest research that you have going show on the idea of a genetic marker for aging? Is the aging process actually dictated in our genes themselves?

Dr. **Williams**. If I may, I would like to ask Dr. Schneider to address this question.

Dr. **Schneider**. I think we are a long way from understanding the aging process. There are many theories. Some of them suggest a genetic component, others a more environmental component. But I think there is very little data right now suggesting anything but that aging is the sum total of both.

LONGEVITY IN RUSSIA

Mr. **Conte**. Is there a town in Russia where the people live over 100 years?

Dr. **Schneider**. Oh, that is a great story. If you wish, I will tell it to you.

Mr. **Conte**. Sure. Claude Pepper tells me about it all the time. [Laughter.]

Dr. **Schneider**. It is in the Georgia area of the Soviet Union where people purportedly live to 130, 140, and even 150 and you see photographs of a man playing the accordion at age 110 and his grandmother is looking down as he plays the accordion.

But Dr. Memvedev in England did a study and researched what, in fact, was the reason for this and he came up with a finding that in the First World War in Russia, in 1914, there was universal conscription: that is, everyone aged 18 to 65 was eligible for the draft.

So all of a sudden people in various out-areas of the Soviet Union, like Georgia, became 65, 70, and 75; and, today, they are 120, 130 and 140. [Laughter.]

There is no evidence that they live any longer.

NUTRITION RESEARCH

Mr. **Conte**. That is a pretty good tale.

You note in your statement that the NIA's research on nutrition attempts to define nutritional requirements for good health in the elderly, how dietary deficiencies are associated with disease, and how eating habits change with age. How much of your budget is specifically devoted to nutrition research?

Dr. **Williams**. That figure is quite modest. This is one area we would like to try to increase.

It is about $4.6 million of our budget right now that has been identified as being involved in nutrition research. This is another very understudied area in older people. We don't have very good data at all, for example on which to base recommended dietary allowances. We are just initiating a special emphasis career award to encourage more people to enter nutrition research.

Mr. CONTE. Two doors down the hall from here, we have another Subcommittee that will meet soon to review the United States Department of Agriculture budget request for nutritional research. Among our most significant achievements in the past couple of years was the establishment of the Human Nutrition Center on Aging at Tufts University in Boston. With Chairman Natcher's strong support, we have created a highly-qualified research team there. We hope to be able to expand their work this year, but we'll be lucky if we can keep the present level of $12 million going. Doctor, what do you think about the work underway at the Tufts Center, and how closely do you work with that research team there?

Dr. WILLIAMS. We keep in close touch with it. I have visited myself. Our Scientific Director, Dr. Greulich, is an ex officio member of the scientific advisory committee reviewing their work and we are in touch with the Department of Agriculture program officers here.

In my own opinion, they are doing some very valuable research. They are doing studies—for example, metabolic balance studies—on older people over time which should help give us, almost for the first time, good data on what it takes to keep older people in metabolic balance: that is, with appropriate nutrition, among other studies.

Mr. CONTE. Besides the Tufts Center, there is a lot of research going on all over the place on nutrition. In your opinion, is the Federal research effort on nutrition and aging well-coordinated? Do you think there is anything that needs to be done to improve it?

Dr. WILLIAMS. I think it is still a field that needs to be expanded in the research devoted to nutrition and aging.

In terms of coordination, I am afraid I don't have a good picture about any overall coordination. We do have an inter-agency Coordinating Committee on Research in Aging which has representation from the Department of Agriculture as well as about 18 other Federal agencies. We attempt to do coordinating there. But I cannot give a very specific answer, I am afraid, on the nutrition field, sir.

Mr. CONTE. I have some other questions and I will summit them for the record.

Thank you, Mr. Chairman.

Chairman NATCHER. Mr. Stokes.

MINORITY LONGEVITY

Mr. STOKES. Thank you, Mr. Chairman.

Dr. Williams, the statistics that have been given to us indicate that both black men and black women die earlier than white Americans.

I am wondering, if those statistics have changed any over the past few years?

Secondly, I understand there is a phenomena that when blacks pass a certain age they then begin to outlive whites.

Is this phenomena still common?

Dr. **Williams.** Yes, sir. That is a very interesting apparent fact. I say apparent because in some of the recent studies it has not been quite as clear and there are some methological questions raised about being entirely accurate about birthdate, age and appropriate selection of the populations studied. Still, the preponderance of evidence, in my judgment, is just as you stated it: that beyond about age 75 it appears that black people may live longer than white, both men and women, and yet at earlier ages we have lots of data to indicate that survival is shorter at earlier ages.

It raises a lot of interesting questions. A simple way to think about it would be that if you survive into late years, you are a survivor by definition and that may characterize an unusually healthy basic condition in the first place.

There is also evidence that some of this may apply, in relation to certain diseases at any rate, in all races. For example, there is evidence that the new incidence of cancer may level off or even actually decline beyond about age 80 in both races, which would suggest, again, a possibility of a survivorship meaning that if you reach a certain age you may be a little better protected against some diseases.

Mr. **Stokes.** What is the longevity differential now between black males and females, and white males and females?

Dr. **Williams.** I can give you precise figures for the record.

Mr. **Stokes.** Please.

Dr. **Williams.** Approximately, for black males, it is just a little bit beyond age 65, the last figures I saw, whereas for white males it is about 71 or so; and for females, I think it is about 70 or 71 for black females and it is almost 80 for white females. I will check those data and give them to you.

Mr. **Stokes.** Sure. Feel free to clarify that for the record.

[Information follows:]

Differential Life Expectancy

The latest available statistics on longevity are based on 1982 provisional data, and were published by the National Center for Health Statistics in *Health U.S., 1983.* According to this data, the average life expectancy for black males is 64.8 years and for black females it is 73.8 years. For white males and females, it is 71.4 and 78.7 years respectively.

INTRAMURAL RESEARCH

Mr. **Stokes.** What major areas of research are conducted in your Institute's Intramural Research Programs?

Dr. **Williams.** In our Intramural Program, Mr. Stokes, we have essentially two major activities. One, is laboratory research carried out mainly in Baltimore, but also at one laboratory in Bethesda. The other is our epidemiology intramural program.

In our intramural laboratories, our largest laboratory, the Laboratory of Neuroscience, is based in the clinical center in Bethesda. It is working on dementia and related problems in older people. Other important areas include our new Laboratory of Molecular Genetics that we have begun in the last year working on molecular genetics in aging and in diseases of older people. Then the other important labs include labs on immunology, on metabolism, and on basic chemical and cellular changes in aging.

All of these are tied together for one common effort, and that is on the Baltimore Longitudinal Study of Aging where, for 28 years now, we have been following a volunteer group of healthy people and following the normal progression of healthy aging. The Baltimore Longitudinal Study is a fundamental resource for information on what aging is like.

Mr. STOKES. Now, you have recently reorganized this Department.

Dr. WILLIAMS. Yes, sir.

Mr. STOKES. What was the purpose of the reorganization?

Dr. WILLIAMS. We had found, through a review, that we needed to have a senior person in charge of this whole Baltimore Longitudinal Study of Aging to help coordinate the various studies better and to make them more available for other scientists to participate in. Up until then, they had been loosely related, but there had been a good bit of autonomy in the way these studies were conducted with this longitudinal population. We now have a very good new associate director specifically in charge of that program to make it a more thoroughly coordinated program, to help us analyze the data more completely, and to invite other scientists to participate.

Mr. STOKES. Dr. Williams, do you establish goals for your senior administrators for addressing minority program and personnel issues?

Dr. WILLIAMS. Yes, sir, in a very general and, I hope, effective way, we do. We make a very major effort to try to see that all of our recruitment opportunities are widely known among minority settings as well as others, but specifically through minority settings, through personal contacts as well as general announcements in advertising.

I, personally, see to it that any minority candidates are thoroughly considered and we have participation in all of our major appointments of equal opportunity employee counselors and we try to take this into consideration in a very thorough way.

We have had some successes in selections this way. Our most recent appointment at a high level was Dr. Herbert Nickens appointed to be Chief of our Office of Program Analysis and Planning. Unfortunately, he recently left us to become head of the Minority Health Office in the Assistant Secretary's office.

Mr. STOKES. I would appreciate it if you would supply for the record the following information: for SES, senior level professional and senior level administrative positions in your Institute; the current number of all such positions and the current number of these positions occupied by blacks.

Dr. WILLIAMS. Yes, sir.

Mr. STOKES. Thank you very much.

[Information follows:]

MINORITY EMPLOYMENT

The National Institute on Aging supports five SES positions, one of which is held by a woman but none of which are black. One of the 15 senior professional and administrative positions, th NIA Assistant Director for Programs, is held by a black woman. In addition, the NIA Equal Employment Officer and the Special Assistant to the Associate Director of the Biomedical Research and Clinical Medicine program, are blacks. The NIA Program Planning Officer, who just recently left to become Director of the Office of Minority Health, DHHS, was also black.

Mr. **Stokes**. Thank you, Mr. Chairman.

Chairman **Natcher**. Dr. Williams, we want to thank you and your associates for appearing before our Committee on behalf of your budget request for the fiscal year 1987.

Doctor, this has been a good hearing. Thank you very much.

Dr. **Williams**. Thank you, Mr. Chairman, and thanks to your committee.

[The following questions were submitted to be answered for the record:]

TRAINING

Mr. Conte. Do you have any estimates, in actual numbers, on what the training needs will be in the coming years?

Dr. Williams. The 1984 congressionally mandated Report of the Health and Human Services Taskforce on "Education and Training in Geriatrics and Gerontology" calls for a doubling to tripling of the yearly numbers of postdoctoral fellows and trainees in order to reach minimally adequate numbers of faculty in the Nation's medical and other health professional schools by the year 2000. Objective Five of the HHS Report on Education and Training in Geriatrics and Gerontology calls for at least 600 investigators -- other than physicians -- to be prepared by 1990, and 1,300 by 2000.

The NIA supported 100 competing extramural FTTPs plus 6 new intramural fellows in FY 1985. We expect to support 48 new intramural and extramural trainees in FY 1986. Taken together, this totals 154 new trainees since the taskforce report was issued. An additional 300 trainees, both intramural and extramural, are currently in the system and will be graduated by 1990. Of the total 454 trainees about 70%, or 318, can be expected to remain in aging research. This leaves a shortfall of 282 required to meet the 1990 goal of 600. To achieve this additional number, approximately 403 additional trainees must be graduated by 1990. Since it normally takes a minimum of three years to train an investigator, all 403 would have to be in the system by 1988. We would, therefore, need to support approximately 202 new trainees per year over the next two years.

GERIATRIC LEADERSHIP ACADEMIC AWARD

Mr. Conte. Can you tell us a little bit about your geriatric leadership academic award program? What is the role and purpose of this program?

Dr. Williams. The Geriatric Leadership Academic Award (GLAA) supports leadership activities in the development of research and research training programs in all aspects of gerontology and geriatrics, i.e., biomedical, behavioral, and social aspects of aging and the special problems of older persons. This award is aimed at encouraging and assisting more health professional schools to increase their efforts in research and training in aging.

Priority is given to those academic centers of schools with limited activities in aging but which have a strong interest in, and commitment to, expanding their research and training efforts in aging. These awards offer opportunities for supporting start-up or expansion of such activities. Thus, this program is aimed at meeting needs which have not been met by other types of awards available from the NIA and Federal agencies.

The development of research activities at the applicant's institution(s) is an essential element of programs to be supported by the GLAA. Teaching programs to be developed under the award mainly include training to impart knowledge and skills needed for aging research.

It is also a goal of the GLAA program to focus emphasis on aging research from a full range of disciplines at an academic institution rather than one discipline. It is especially important for programs to involve research by basic science departments, and to foster research collaboration between basic and clinical investigators.

DIETARY SUPPLEMENTS

Mr. Conte. Your statement says that 90 percent of all women have osteoporosis by age 85. Last week we had the National Cancer Institute in here testifying once again on the benefits of consuming more fiber. Do your studies show any link between fiber consumption and the body's ability to absorb calcium?

Dr. Williams. There are studies which indicate that some types of fiber interfere with calcium absorption. However, other studies in persons consuming diets adequate in calcium found no evidence that fiber significantly impaired absorption. A major problem in resolving this issue is that there are many different types of dietary fiber -- different types of brans, cellulose, pectins, and many more. Their effects on calcium absorption may vary widely. At present our knowledge of the health effects of each of these different types of fiber is primitive -- analogous to our understanding of cholesterol forty years ago. Progress on this topic is important in view of the significant health effects of fiber in the diet.

Mr. Conte. There seems to be widespread agreement that calcium supplements can reduce the occurrence of osteoporosis in women. Is there any evidence that these same calcium supplements impair the body's ability to absorb iron?

Dr. Williams. This is an interesting question. Many calcium supplements cause diminished stomach acidity. This can cause impaired iron absorption. While most persons probably can secrete enough stomach acid to compensate for this effect, some may not. This is of special concern for older people, among whom impaired stomach acid secretion is quite common. Thus, as use of calcium supplements in large doses becomes more common, we need to know more about their effects on iron metabolism in the older population. It is also helpful that after menopause iron requirements are lower.

Mr. Conte. Are there any specific recommendations you would make in terms of diet or general health that our senior citizens should know about?

Dr. Williams. Two dietary concerns are particularly important. The first concerns calcium. Despite the legitimate concerns about possible side effects of increased calcium in the diet, our best estimate is that it would be beneficial for women to consume at least 1000 milligrams of calcium per day for prevention of osteoporosis. This is far greater than the level of about 500 milligrams per day, which is the national average for older women. We still need to know more about the optimal intake of calcium for older women and older men, who are also susceptible to osteoporosis in their seventies and eighties.

A second concern is the adequacy of vitamins and minerals in the diets of older persons. Older persons tend to eat considerably less than they did when they were young. While they may need fewer calories, it is not clear their needs for vitamins and minerals are diminished. Thus their decreased food intake places them at risk for nutritional deficiencies. It is important for older persons to pay attention to the content of vitamins and minerals in their diets to assure adequate intake.

One of our problems in deciding what constitutes an adequate intake of specific nutrients for older persons is that most of the recommendations have been based on studies on young people and may not be appropriate for the elderly. Developing Recommended Dietary Allowances that are appropriate for older persons is an NIA priority.

GENERAL BUDGET

Mr. Roybal. The bottom line on the proposed budget is $145.8 million. What was the total that you proposed in the original NIA submission to Dr. Wyngaarden? What amount did Dr. Wyngaarden use for NIA in calculating his total request to the Public Health Service? What amount did PHS request for NIA from the Department, and the Department from OMB?

Dr. Williams. The original NIA submission to Dr. Wyngaarden was $194.6 million. The NIH submission to PHS and subsequent NIH estimate submitted by PHS to the Department was in the aggregate only. Once the Department had given NIH a total request level, this was spread back across the NIH Institutes. The Department request to OMB for NIA thus became $167.6 million.

Mr. Roybal. How many new grants are you planning to fund in 1987 and how does that number compare to 1985 and 1986 (before and after Gramm-Rudman-Hollings)? How much more would be required to bring the number of new grants back up to the 1986 enacted level?

Dr. Williams. We expect to fund 145 new and competing research project grants under the FY 1987 President's budget. This compares with 209 in FY 1985, an estimated 201 at both the FY 1986 appropriation and sequestration levels, and 177 at the revised FY 1986 level. An additional 56 competing awards would be required in FY 1987 to match the FY 1986 enacted level.

Mr. Roybal. How will the 1987 reduction of $5 million below the 1986 post-sequestration budget and $12 million below the enacted 1986 level affect NIA intramural and extramural program and operations?

Dr. Williams. The intramural program has a small increase -- about 2% -- from the sequestration level. This amount will partially offset the increased costs of such items as maintenance contracts; rent, communications, and utilities; and mandatory personnel compensation increases for within grade increases, promotions, and personnel benefits. The level of research activity will therefore decrease slightly from FY 1986 to FY 1987.

In the extramural program, most of the decrease -- $4.5 million to be exact -- from FY 1986 to FY 1987 will be absorbed by research project grants. This will be accomplished by supporting 56 fewer competing awards and by reducing awards, both competing and noncompeting, below their full recommended levels. Reductions in the centers line will be absorbed by existing grants; other grant mechanisms will be reduced by cutting the number of competing awards. Training FTTPs will be reduced from a total of 230 in FY 1986 to 195 in FY 1987.

Mr. Roybal. The 1987 budget request for grant and center awards includes downward negotiation (10.4% for competing grants, 8.6% for noncompeting, and 9.4% for the centers) from the level recommended during the peer review process. In general, what impact will reductions of this magnitude have on the breadth of scientific objectives, the ability of the study to draw conclusions, or number of years required to complete the research?

Dr. Williams. In the case of ongoing research, cuts of this type will require that personnel and/or staff time allocated to specific projects be reduced and may require deferred purchase of supplies and equipment which had been planned for FY 1987. Competing grants would necessarily be required to reduce the scope of their research from the beginning. The overall effect would be a slowing of research progress and an inability to take advantage of the many new opportunities currently available in the field of aging research.

IMPLEMENTATION OF GRAMM-RUDMAN-HOLLINGS CUTS

Mr. Roybal. Some Federal agencies have reported difficulty in implementing the Gramm-Rudman-Hollings cuts because they did not have the flexibility they needed. Have you experienced problems related to this inflexibility issue and, if so, how has it affected your ability to manage the NIA resources to the best scientific advantage?

Dr. Williams. Policy guidelines required that the 4.3% cut be applied equally across all mechanisms, therefore no specific mechanism (research grants, training, contracts, etc.) was cut more than any other. Research programs (as opposed to research mechanisms) will be affected differentially. For example, Alzheimer disease research supported through research project grants will be maintained at the highest possible level. This will be accomplished by reductions in other program areas which are of lower priority than Alzheimer disease research. By contrast, Alzheimer disease research supported through center grants, specifically the Alzheimer Disease Research Centers (ADRCs), cannot be protected in the same way as almost the entire dollar amount in the centers line is devoted to ADRC funding.

The NIA intramural program will be particularly impacted. Given the intramural budgetary structure and the existence of fixed costs which do not respond to declines in the level of research activity, certain types of expenditures must bear a disproportionate share of the reduction. This category includes the purchase, repair, and maintenance of equipment, essential laboratory supplies and chemicals, professional services, travel, training, professional journals and books, and payment for research volunteers. Although reductions are planned to be taken across the board, the Institute has the authority and flexibility to propose reallocations as scientific opportunities and priorities become clear during the year.

EFFECT OF BUDGETARY CUTS ON SPECIFIC PROGRAMS

Mr. Roybal. What effect on program will sequestration and current budget proposals have on the 7 teaching nursing homes, the Alzheimer disease registry, the NIA initiative on the oldest old, the comparative study of varying ethnic and racial populations, and the clinical trial to study systolic hypertension in the elderly? Please provide the funding levels for 1985, 1986 (sequestration and rescission), and 1987 for each of these five programs.

Dr. Williams. NIA intends to continue support for all its currently funded Teaching Nursing Homes (TNHs) in FY 1986. The first two TNHs, funded in FY 1982, will enter the last year of their 5-year awards in FY 1986. Both have successfully conducted important research projects and are expected to submit competing renewal applications for funding in FY 1987. However, it is likely that funds will not be sufficient to support both these TNHs, and that the number of TNH projects will drop to six in FY 1987. Funding for the teaching nursing home program was $5.2 million in FY 1985. It is estimated at $4.8 million and $3.9 million for FY 1986 and FY 1987 respectively.

In FY 1986, the Congress appropriated $2.5 million to the National Institute on Aging (NIA) for the purpose of establishing an Alzheimer Disease Patient Registry. The NIA has issued a Request for Applications. The total amount that will be available for the Registry after the sequestration is $2.4 million.

Progress on the oldest old has been slow. Some data are being collected through the NIA population contracts. The NIA issued a program announcement in December, 1984, soliciting research proposals on the oldest old, but only now are fundable applications being received. The topics covered by currently funded research grants include demographic analyses of multiple causes of death, the demography of the extreme aged, trends in morbidity, and the changing composition of the oldest old. It is expected that at least two more projects will be funded during the remainder of FY 1986. In FY 1985, funding for research on the oldest old totalled about $808,000. It is expected to increase to about $1.3 million in FY 1986 and will remain essentially stable in FY 1987.

In 1984, the National Institute on Aging awarded a competitive contract to Duke University entitled, "Established Populations for Epidemiologic Studies of the Elderly," to establish a population to study older blacks. This population will be followed for five years through two household interviews and telephone callbacks to collect information on risk factors for disease, measures of health status, and prevalence and incidence of disease. Several important problem-related studies which have been planned for this study will not be initiated at current budget levels. These studies include a study on vision and hearing problems in black elderly, perceptions among black elderly of the attitudes of health care providers in the community, and cancer and pre-cancer of the skin in black elderly. This contract was funded late in FY 1984 for $1.5 million to cover a 2-year period. It is expected to cost at its current level of activity, $843,000 in FY 1986 and $1.1 million in FY 1987.

The clinical trial on systolic hypertension in the elderly was begun in FY 1984, after pilot studies had proved its feasibility. Considerable effort and a significant amount of fiscal resources have been expended on this trial, and there is currently no plan to reduce it below committed levels. Funding for this trial was $4.0 million in FY 1985 and is estimated at $4.0 and $3.1 million in FY 1986 and 1987 respectively.

RESEARCH ON FAMILY SUPPORT FOR THE ELDERLY

Mr. Roybal. Concern is growing for the stress which is placed on those who are providing care for the victims of Alzheimer disease, as well as for families dealing with any chronic, degenerative

disease or functionally impaired "oldest old." How many awards is NIA funding for studies on family support for individuals with Alzheimer's disease or other chronic diseases and on the stress on those caregivers? Please provide the number of awards and associated dollar level spent in 1985 and planned for 1986 (sequestration and rescission) and 1987 for these activities.

Dr. Williams. It is well established that the family is the major source of emotional support and care of older people. Yet the family itself is undergoing many changes: increasing longevity has revolutionized the structure of the family so that for the first time in history four, even five, generations of a family are alive at the same time. Other changes affecting the family system are the decline in fertility, the growing fraction of women in the labor force and in the older population, and high levels of divorce and remarriage. NIA supports research on how these changes will affect intergenerational relationships, influence the family's support capabilities, and reinforce or change the norms of independent housing and of new roles for women.

Some specific topics recently addressed by NIA-supported research include projections of kin available to provide caregiving, studies of intergenerational relationships in the broad population and in specific ethnic and racial groups, patterns of community care and social support provided to frail older people, ways of enhancing caregivers' capacity to care for older relatives with Alzheimer disease and other medical and behavioral problems, and conflict, abuse and neglect involved in the family care of older people.

In FY 1985, NIA supported approximately 10 projects which address the provision of care by family members to Alzheimer disease patients or other chronically ill or frail older people at a funding level of somewhat more than $1 million. We expect to support a similar number of projects for approximately the same amount under the current NIA budget for both FY 1986 and FY 1987.

ALZHEIMER DISEASE

Mr. Roybal. What are the most promising scientific opportunities today in the study of Alzheimer disease?

Dr. Williams. The most promising scientific opportunities in the study of Alzheimer disease (AD) include the following general areas of research.

- Improvements in diagnostic screening instruments and tests for early and accurate diagnosis of AD. These tests include new neuropsychological test batteries, detection of abnormal proteins in the blood, identification of metabolic disorders linked to the disease, and finding specific genetic markers linked to familial cases of Alzheimer disease.

- Rapid advances are possible in finding the cause(s) of AD through systematic studies of families that have an unusually high number of affected members. Modern molecular biology has the tools for finding the biological cause of AD. Recently it has been shown that cells from AD patients have defective transport mechanisms. Scientists are on the verge of finding out what causes the formation of abnormal protein in the brains of AD patients.

- In the arena of treatment, one of the most promising areas is the possibility that lost brain function can be reversed by transplanting the appropriate type of nerve cells. Work in this area has been successful in animals. It has been shown that old brains make excellent hosts for nerve cell grafts. This kind of work promises to provide a real treatment for the symptoms of AD.

Mr. Roybal. To what extent are you pursuing these avenues of research in the diagnosis, treatment, and prevention of this disease?

Dr. Williams. One of the major problems that impedes the progress of research in AD lies in the accuracy and sensitivity of diagnostic procedures. Recent major workshops on this topic, organized by NIA with multiple sponsorship, have helped to define the diagnostic issues and specify research opportunities in this area, including the identification [illegible] plasma protein that can be used as a marker for AD; the possibility of locating membrane transport abnormalities in peripheral nonneural tissues; the development of better correlations between cognitive measures and data from brain imaging devices such as Nuclear Magnetic Resonance and Positron Emission Tomography; and the construction of more sensitive neuropsychological test batteries for detecting memory loss.

In the area of treatment, recent research by several groups supported by NIA has shown the previously unrecognized plasticity of the central nervous system and has begun to identify trophic factors and chemical messengers regulating nerve growth in the aging brain. With further progress in this area, the prospect of treating AD becomes a realistic goal.

Research supported by NIA and other institutes related to prevention includes the role of familial (genetic) factors in some cases, the role of head trauma, and the likely role of very high intake of aluminum.

Mr. Roybal. Please provide funding levels and number of awards by mechanism for 1985, 1986, and 1987, and comment on specific programmatic effects of any budgetary reductions proposed for 1986 and 1987.

Dr. Williams. At the FY 1986 Appropriation and sequestration levels, the NIA would have expected to fund approximately 99 Alzheimer disease research grants including the 10 Alzheimer Disease Research Centers. This drops to 95 awards under the revised FY 1986 budget. The number of training and contract awards remain the same at all three FY 1986 levels, but will be negotiated down about 4.3% from the Appropriation level. The Laboratory of Neurosciences will be reduced $226,000 below the FY 1986 Appropriation level of $5,237,000. The total decrease for Alzheimer disease research from the Appropriation level of $34,048,000 is $1,954,000.

These decreases will slightly lower the number of Alzheimer disease grants which can be supported. The downward negotiation of competing and noncompeting awards below full recommended funding levels will, in general, slow the progress of Alzheimer disease research. The Alzheimer Disease Research Centers will be affected, as they are already being funded below recommended levels. Intramural Alzheimer disease research will also be affected. The following options are under review for taking this reduction: stopping all studies of familial Alzheimer patients who live outside the Washington metropolitan area to conserve patient transportation funds; reducing use of positron emission tomography (PET) to examine cerebral functional activity; halving the size of the Down syndrome cohort; eliminating a contract to develop methodology to interpret and analyze nuclear magnetic resonance and positron emission tomography data; and significantly reducing computer costs and data analyses.

Despite decreased funds available under the FY 1987 President's budget, we would expect to maintain Alzheimer disease research at the FY 1986 revised levels. This will be accomplished by reducing support in lower priority areas. A detailed table follows.

NIA Alzheimer Disease Research

	FY 1985		FY 1986 Revised		FY 1987 Estimate	
	Proj	Amount	Proj	Amount	Proj	Amount
Res. Grants 1/	89	$22,144,000	95	$23,024,000	95	$23,024,000
Training	5	316,000	6	361,000	6	361,000
Contracts 2/	10	1,301,000	11	3,698,000	11	3,698,000
IR 3/	18	5,069,000	18	5,011,000	18	5,011,000
TOTAL	122	$28,830,000	130	$32,094,000	130	$32,094,000

1/ Includes 10 Alzheimer Disease Research Centers
2/ Includes 2 Alzheimer disease contracts plus 8 contracts with varying percentages related to Alzheimer disease research in FY 1985. The additional contract in FY 1986 and FY 1987 is the Alzheimer Disease Registry.
3/ Includes the entire NIA Laboratory of Neurosciences

Mr. Roybal. Have we exploited the best research opportunities adequately or are some still underfunded?

Dr. Williams. Areas needing further emphasis include: improved diagnostic procedures such as more reliable and accurate psychological tests; work on the metabolic disorders related to AD, especially those that occur in tissues outside the brain; and research on nerve growth, regeneration and chemical messages that enable successful grafting of neural tissue.

Additional work could be done on comparative, longitudinal, community-based studies of dementia that can provide clues to etiologies, define risk factors, delineate differing clinical features, and assist in the development of the strategies for early recognition. While the NIA currently supports several population studies on AD, a number of opportunities exist for utilizing other established demographic and epidemiologic studies to obtain information on prevalence and characteristics of AD and to extend such efforts into comparative cross-cultural international studies.

Mr. Roybal. What level of funding would be required to take real advantage of the most promising avenues of productive research, while insuring that the money would be spent wisely?

Dr. Williams. The level of funding needed to take advantage of these opportunities is difficult to predict. No one knows when or at what level of funding a major breakthrough will occur. However, it is clear that many projects in these areas of research remain unfunded despite very good evaluations of scientific merit by the peer-review system.

Mr. Roybal. How close are we to finding a definitive diagnostic test for Alzheimer disease?

Dr. Williams. During the past few years the medical scientists' ability to diagnose AD has improved significantly. However, at present there is no fool-proof diagnosis of AD. Many investigators are struggling to find a unique biological or diagnostic marker for the disease. Recent major workshops on diagnosis of Alzheimer disease, organized by NIA with multiple sponsorship, have helped to define the diagnostic issues and specify research opportunities which are ripe for exploitation. Important progress has been made in identifying the precise composition of the abnormal proteins in the brain cells of Alzheimer victims, and scientists are now testing if these abnormal proteins can be detected in blood and cerebral spinal fluid from AD patients. Dr. Marilyn Albert, at Harvard University, in collaboration with Dr. Moss, has developed a new neuropsychological test. The test has been administered to a variety of patients with neurological disorders. this test seems to be of great value in the clinical diagnosis of AD. The results of this test have shown that AD patients have a significantly greater loss of information after a brief delay than other patient groups.

Mr. Roybal. Is there adequate research in that area?

Dr. Williams. We have made significant progress in this area and will continue to do so at the levels budgeted.

Mr. Roybal. How will a diagnostic test be useful?

Dr. Williams. An accurate and sensitive test will help physicians to distinguish AD from other conditions which may mimic it, at least some of which may be treatable. This would help reduce the amount of unnecessary institutionalization, with consequent savings in nursing home care costs and reduced pain and suffering for both victims and their families. It would also allow doctors to know whether the dementia they are observing is a treatable form or not. An accurate diagnostic test would also help scientists to pursue research on this condition and allow evaluation of drug therapy and other interventions.

ALZHEIMER DISEASE RESEARCH CENTERS

Mr. Roybal. What effect will sequestration and the 1987 budget proposal have on funding for the 10 Alzheimer Research Centers authorized by the Congress? How many fewer centers will be funded? If all 10 are funded, what level of funds will be allocated to each?

Dr. Williams. The Alzheimer Disease Research Centers (ADRCs) have never been supported at full recommended levels. The sequestration will further reduce the funds available for the ADRC. Typically, the ten ADRC have delayed the start of pilot projects. These projects are designed to provide start-up funds for a new idea or serve as a quick way of checking the validity of a hypothesis. Another strategy used by the ADRC has been to reduce the number of patients being studied. At the Harvard University ADRC, several projects which were scheduled to start in FY 1986 are being delayed. These include the following: a project which has an overall goal of determining whether there are subgroups of patients within the classification of AD; a project to study the chemistry of neurofibrillary tangles, the primary brain pathology in AD; and a project to attempt to isolate a specific and unique DNA fragment from the genome of patients identified s manifesting familial AD. The availability of such a DNA marker could allow improved and even presymptomatic diagnosis of the disease. This project eventually might lead to isolation and characterization of the defective gene and gene products.

The University of Southern California ADRC had expected to study 13 patients per year including clinical assessment with a final autopsy. Because of the tremendous desire of the family members to enroll in these studies, they have had over 40 patients during their first year of study and have a large number of brains which have been obtained for neuropathological studies. At current funding levels, expansion of this project could not be accomplished, thus delaying the opportunity to compare the pathological findings with clinical data on these patients.

All ten ADRCs will be funded in FY 1987. The total available for centers, including the ADRCs, is $9.8 million. The specific amount for each center has not yet been determined.

Mr. Roybal. How much is required to fund all 10 centers at full capacity?

Dr. Williams. Total full cost for centers, including the 10 ADRCs, is estimated at $12.3 million.

ALZHEIMER DISEASE RESEARCH

Mr. Roybal. What is NIA doing to insure coordination and timely exchange of information in the field of Alzheimer disease research and patient management?

Dr. Williams. The NIA Information Office has built a strong public education program focusing on changing public needs related to Alzheimer disease: first, helping the public to recognize that senility is not a part of normal aging; next, helping them recognize and identify Alzheimer disease; now, helping to spread the latest information on what might cause the disease, how it progresses and what can be done to help the patient and the family; and, as it becomes appropriate, spreading the word on how the disease can be cured and prevented. With these goals in mind, our information and our educational materials on Alzheimer disease have been distributed to several million individuals -- through NIA distribution channels as well as through the Alzheimer's Disease and Related Disorders Association (ADRDA), the American Association of Retired Persons, and major national and local media.

We are particularly excited about the Alzheimer Disease Research Center (ADRC) program and by the opportunities this program presents to translate research advances into improved care and diagnosis of Alzheimer patients. In order to insure the timely dissemination of information, and to develop new means of translating the latest information on Alzheimer disease, we have recently begun talks with public affairs experts at several of the ADRCs. It is our plan that the 10 currently funded ADRCs will work together -- and will develop ties to local ADRDA chapters -- to form a strong national network to coordinate public education activities in the area of Alzheimer disease.

Mr. Roybal. Are other countries experiencing the same problem with Alzheimer's disease that we are in this country?

Dr. Williams. Almost all developed or developing countries, which have the same life expectancy as this country, have the same social and economic problems associated with Alzheimer disease. However, in some countries, because of their long established cultural and institutional traditions, caring for AD patients is handled in a manner that poses less of a burden on the families than in this country.

Mr. Roybal. Is NIA involved in any international comparative studies or scientific exchanges, and what do you perceive as the value of such research?

Dr. Williams. The NIA has made an effort to stimulate cooperative studies with other countries. The Institute works closely with the World Health Organization (WHO) and the Pan American Health Organization (PAHO). We have sponsored a joint conference with WHO on international diagnostic standards for AD. International collaborative studies must be planned with great care because cultural differences make some of the diagnostic instruments and tests invalid for cross-cultural studies. We are in the process of building such instruments and bridges with other countries. The value of such longitudinal epidemiological studies is beyond measure because they promise to provide clues about differential risk factors, and they may shed light on the possible effects of genetics, nutrition, toxins and social factors in the causation of AD.

TRAINING IN GERIATRICS

Mr. Roybal. Has the DHHS intra-agency committee on geriatric training met to discuss the impact of current Departmental proposals related to geriatric training, including the proposal to eliminate the HRSA Health Professions Program and the ADAMHA clinical training program and to significantly reduce the number of NIA training awards? What is the group's assessment of how these proposals would affect geriatric training in this country, and the ability of the academic institutions to carry on the same level of effort without the direct Federal assistance, while they are also absorbing the proposed Medicare reductions for medical education reimbursement?

Dr. Williams. The HHS Task Force on Enhancement of Geriatrics and Gerontology met January 7, 1986. When the group met in January, the FY 1986 budgets of the representative_agencies were not known because of the effects of the sequestration. Thus, the specific issues of the HRSA Health Professions and ADAMHA Clinical Training Programs were not addressed. Insofar as the NIA is concerned, the total number of NIA extramural Research Career, Individual, and Institutional positions will decline from 306 in FY 1985 to 300 in FY 1986 and to 263 in FY 1987. At the same time, the number of new and competing extramural trainees will decline from 100 in FY 1985 to 42 in FY 1986, then increase slightly to 47 in FY 1987. Intramurally, the NIA is currently supporting 35 staff fellows and medical and senior staff fellows. Approximately the same number will be supported in FY 1987.

The Institute, in collaboration with HRSA and in cooperation with the HHS Task Force, expects to undertake the response to the directive in the Health Research Extensions Act (PL 99-158) which is to conduct a study and develop a report on "Personnel Needed for Health Care of the Elderly."

CONTINUING CARE

Mr. Roybal. To what extent is NIA currently funding research and training in continuing (long term) care -- particularly as it relates to the chronic care needs of the oldest old and to victim's of Alzheimer's disease? Are such activities within NIA's purview and capacity?

Dr. Williams. There are many research issues in the area of formal health care for older people which are in the purview and capacity of NIA to support. The Teaching Nursing Home Program is one of NIA's major programs for research on chronic care needs of the elderly. Current funding for the TNHP is about $4.8 million. As stated earlier, NIA spent somewhat more than $1 million in FY 1985 for research grants on the informal or family care of older people. In addition to this, the Behavioral Sciences Research program is also supporting approximately 8 projects having to do with patterns of institutionalization and nursing home care for older people for a cost of approximately $1 million.

The NIA provides funds for training through its ADRC program. The Alzheimer Disease Research Centers also are mandated to conduct other educational activities for health care providers through continuing medical education programs. The Centers are designed to serve as national resources for training of professionals and paraprofessionals in health care delivery. These activities do take place at the Centers, the funds for these programs often are provided from other sources.

Mr. Roybal. What types of research and training are needed to improve service delivery and adequately meet the continuing care needs of older persons? What level of funding would be needed to support such activities?

Dr. Williams. Many of the continuing care needs of the elderly stem from the lack of effective treatments for many of the debilitating conditions of late life, such as osteoporosis, urinary incontinence, osteoarthritis, and dementia. Research in the Teaching Nursing Home program focuses both on better understanding of these diseases and testing of new treatments. There is enough interest and expertise in the research community to justify support for at least eight TNHs in FY 1987. This would require expenditures of approximately $5.7 million per year, an increase of $0.9 million above the FY 1986 level of support for this program.

During FY 1985, a workshop on aging and formal health care sponsored by the NIA Behavioral Sciences Research program in collaboration with the National Center for Health Services Research focused attention on four broad research areas: antecedents of health care utilization among older people; patient-provider interaction; the organization and functioning of particular health care institutions (e.g., hospitals, home health care, nursing homes); and social and behavioral aspects of institutionalization. NIA staff has planned to issue a program announcement in the area of aging and formal health care to encourage more research here. Currently, the NIA is spending approximately $1.0 million in this area, and twice as much could be adequately spent.

Mr. Roybal. NIMH and the Administration on Aging are also conducting research on the chronic care needs of persons with Alzheimer and other disorders. To what extent is the work of NIA coordinated with these other agencies?

Dr. Williams. The programs of NIA and other agencies supporting research on long term care for older people are largely determined by our respective mandates and missions. NIA supports research that extends the knowledge base underlying the provision of health services for the aging and the aged. NIA does not support demonstration or evaluation projects except as these may be built into systematic and generalizable studies that are clearly grounded in relevant theory and designed to add to the scientific knowledge base. The program of the National Institute of Mental Health is geared to mental health issues. The Administration on Aging is able to support evaluation and demonstration projects which are beyond the mission of the NIA. Our staff and the staff of these other agencies refer applicants to each other when a proposed project seems inappropriate for a particular agency.

The NIA staff work in close collaboration with the staff of AoA and NIMH in all areas of research relating to Alzheimer disease when there is a mutual interest. Such collaboration takes many forms: personal contacts, clearance of program announcements, joint planning of meetings and conferences, and co-funding of projects.

OSTEOPOROSIS

Mr. Roybal. What is the estimated prevalence of osteoporosis in this country? Are there regional or racial and ethnic differences in its distribution?

Dr. Williams. Osteoporosis affects at least 15 to 20 million persons in the U.S. Though it is more common in women, many older men have osteoporosis. The fact that osteoporosis is mainly a disease of older people is reflected in the fact that 84 percent of the more than 200,000 hip fractures per year in the U.S. occur in persons over 65, mainly as a result of osteoporosis.

There has been speculation that there may be important regional differences in the prevalence of osteoporosis. Because vitamin D is important in maintaining bone density, and because this vitamin is made in the skin in response to sunlight, it is thought that age-adjusted rates of osteoporosis may be lower in the southern states. However, we still need good epidemiologic data to answer this question, which is important since it could help us evaluate the benefits of vitamin D in preventing osteoporosis.

It has been known for some time that black women are at less risk for osteoporosis than white women. The causes for this are still largely unknown. It would be important to learn them, since they could give clues to protective factors against this disease. Other ethnic factors may be important, but need to be sorted out from the effects of diet and environment.

Mr. Roybal. How have or will the research on osteoporosis be affected by current budget proposals, in terms of the number of projects and the funding in 1985, 1986, and 1987?

Dr. Williams. The current budget proposals will not fund all meritorious projects on osteoporosis. In FY 1986, NIA funding for osteoporosis and related research may drop slightly from the FY 1985 level of approximately $6 million, with further reductions in FY 1987.

Mr. Roybal. What effect will the budget proposals have on the development of effective treatment?

Dr. Williams. The NIA has planned an initiative in cooperation with the National Institute of Arthritis and Musculoskeletal and Skin Diseases for FY 1987. The initiative will fund comprehensive research programs on the causes, prevention, and treatment of osteoporosis at academic medical centers. It is titled "Programs of Excellence of Research on Osteoporosis." We believe there is sufficient research expertise to support at least six centers in FY 1987. The total one-year cost for NIA for six awards is estimated at $7.0 million, however NIA will be able to fund only two Programs of Excellence of Research on Osteoporosis for an estimated total cost of $2.25 million per year.

There are many promising leads for better treatments, including new types of estrogen therapy and Vitamin D derivatives. Results from research on bone metabolism suggest other new approaches that may be even more effective. Because of large number of factors that affect bone density, these treatments need to be tested in centers with the capacity to evaluate all their effects. Most research grants in this area do not support such comprehensive approaches. The Programs of Excellence of Research on Osteoporosis would fill this need and allow definitive testing of new treatments and preventive approaches.

FY 1986 RESCISSION

Mr. Early. In answer to one of my questions to another institute I was told the amount of the rescission being proposed for that institutes had been "assigned" to it. Doctor, what I'd like to know is, how were the institutes selected for a rescission (some institutes do not have rescissions)? Also, how was the amount of the rescission for your institute arrived at?

Dr. Williams. While the total amount of the FY 1986 rescission for research project grants was mandated by OMB, the Office of the Director, NIH, had the responsibility of allocating the total reduction and assigning specific rescission amounts to each Institute. The amount of each Institute's rescission was determined in two steps. First, a simple proration of the total rescission was computed against each Institute's funding for research project grants. Then these amounts were adjusted further to reflect NIH research priorities.

Mr. Early. In your professional judgment, overall what kind of an impact would this rescission ($2.679 million) in addition to the $6.729 million sequestered, have on your programs in FY 1986?

Dr. Williams. Our competing research project grants would drop from 201 provided by both the FY 1986 appropriation and the sequestration to 177. This would drop our award rate from 34.5% to 30.4%, and reduce funding for important but lower priority research programs. Priority research will be protected to the extent possible.

Mr. Early. Under the FY 1986 enacted level, NIA would be able to fund 201 new and competing research grants. Under the Administration's revised FY 1986 proposal NIA would fund only 177 or 24 fewer? Doctor, tell us briefly, what areas of research would be affected by this reduction?

Dr. Williams. On-going, high priority research -- Alzheimer disease, osteoporosis, and molecular genetics -- would be reduced somewhat from the enacted FY 1986 level. Research grant funds for Alzheimer disease would, for example, decline $1.0 million, or about 4.0 percent. This decrease would result in three to four fewer Alzheimer disease research grants. Research grant funds would decline about the same percentage for osteoporosis and molecular genetics. New initiatives, such as molecular genetics, studies of the oldest old and research on neuroendocrine factors in the aging immune system would be slowed. Lower priority areas such as pharmacology and studies of gastrointestinal problems would be cut to provide adequate support to NIA's highest priority research.

FY 1987 REQUEST TO NIH

Mr. Early. What was the Institute's budget request to the Office of the Director?

Dr. Williams. The NIA's FY 1987 request to NIH was $194.6 million.

FUNDING RATE

Mr. Early. What percentage of approved grants would be funded under the FY 1986 revised budget request? How does this compare to your original FY 1986 estimate? How does it compare to FY 1985?

Dr. Williams. Under the FY 1986 revised request, the NIA would fund approximately 30.4 percent of approved applications. The FY 1986 estimate at the original, enacted level was 34.5 percent. In FY 1985, 32.3 percent of approved applications were awarded.

EFFECT OF DOWNWARD NEGOTIATIONS

Mr. Early. According to the budget justification there will be downward negotiations of 10.4% and 8.6% in competing and non-competing grants, respectively. Will each grant be reduced by these amounts?

Dr. Williams. These reductions are not intended to be applied across-the-board. Each grant will be reviewed on an individual basis.

Mr. Early. What impact will reductions of this size have on the Institute's research activities?

Dr. Williams. The proposed reductions would result in less research being accomplished than would have been possible at the full funded level. This will, especially if such reductions are continued in future years, slow the progress of aging research generally, reduce our ability to pursue new research opportunities in a timely manner, and delay implementation of the practical applications which will result from this research.

Mr. Early. In your professional judgment, Doctor, do you have any serious concerns about the size of the downward negotiations the project grants are being forced to take under this budget request?

Dr. Williams. The proposed downward negotiations are of serious concern. While they will not halt on-going aging research, they will inhibit its progress and delay implementation of new initiatives.

Mr. Early. The budget indicates that direct costs for research centers will be reduced by 9.4% in FY 1987, compared to 4.3% in FY 1986. Are reductions of this size something we need to be concerned about?

Dr. Williams. Since inception of the ADRC program, these centers have never been supported at the full recommended funding level. Most ADRC Directors have chosen to minimize the effects of these short-falls by delaying the hiring of personnel essential to some projects, delaying the purchase of some equipment, postponing the start of some projects, and/or reducing the number of patients being studied or recruited for the clinical studies.

The reductions in FY 1986 and FY 1987 will add to this situation, with currently unfunded projects likely to remain unfunded and special opportunities arising from on-going research being delayed.

Mr. Early. What effect will these reductions have on the research programs at these centers.

Dr. Williams. They will further reduce the level of effort which these centers can support and require that currently unfunded ADRC subprojects remain unfunded.

Mr. Early. How will the reduction in the size and scope of the centers program affect NIA's program plans -- both immediate and long range?

Dr. Williams. While the scope of on-going centers will have to be reduced to some degree below current funding levels, the principal impact will be on lost opportunities. The Alzheimer Disease Research Centers, for example, will not be able to take advantage of their full potential, including the prospect for multicentered national studies on the causes of Alzheimer disease and clinical trials utilizing Alzheimer disease patients. In the long run, the reduced scope of these centers will slow research progress, thus delaying an understanding of the causes of Alzheimer disease and development of diagnosis and treatment methodologies.

CENTERS

Mr. Early. How many centers will be up for renewal in FY 1987? Provide the names and locations of these for the record.

Dr. Williams. None of the Alzheimer Disease Research Centers will be renewed until 1989. One other center will be up for renewal in FY 1987. This is a core center at Duke University, Durham, North Carolina, which provides centralized research support services to NIA-supported research grants in that vicinity.

CLINICAL TRIALS

Mr. Early. Were any new clinical trials started during FY 1986? If any new ones were started, please provide a list.

Dr. Williams. The NIA did not start any new clinical trials in FY 1986.

Mr. Early. How many clinical trials are underway in FY 1986? Provide a list of the clinical trials underway in FY 1986, and indicate their associated cost.

Dr. Williams. Two major clinical trials are underway in FY 1986. The NIA, in conjunction with the Division of Nursing, PHS, is cofunding a clinical trial on urinary incontinence in the older population. The total estimated cost for this clinical trial in FY 1986 is $1.2 million. The split between NIA and the Division of Nursing varies from year to year, but each agency will ultimately pay 50 percent of the total projected cost of the trial -- estimated at $4.2 million. The clinical trial on systolic hypertension in the elderly, co-funded with the National Heart, Lung, and Blood Institute, will cost each Institute approximately $4,000,000 in FY 1986.

Mr. Early. Will you have to curtail any ongoing clinical trials with your FY 1986 revised budget request? If so, which ones?

Dr. Williams. The NIA has invested both a considerable effort and substantial resources in these two clinical trials. At the present time we have no plans to curtail either of them.

Mr. Early. Doctor, will you have to curtail any ongoing clinical trials with your FY 1987 budget request? If so, which ones?

Dr. Williams. We do not expect to curtail either the urinary incontinence trial or the systolic hypertension trial in FY 1987.

Mr. Early. Will you be able to start any new clinical trials in FY 1987?

Dr. Williams. The NIA has no plans for new clinical trials in FY 1987.

Mr. Early. Are there any high priority clinical trials which are ready but cannot be initiated because of lack of funds in the FY 1987 request? If so, please provide a list of these, along with a brief description and the associated costs, including first year costs.

Dr. Williams. At the present time, the NIA has no new clinical trials planned.

SMALL BUSINESS INNOVATIVE RESEARCH

Mr. Early. Doctor, is your Institute utilizing the Small Business Innovative Research program? If so, for the record provide an explanation of how NIA is taking advantage of this program.

Dr. Williams. The NIA is participating in the Small Business Innovative Research program. In response to the NIH Small Business Innovation Research (SBIR) solicitation for grant applications, NIA receives and assigns such applications. The NIA is sensitive to the importance of promoting and utilizing small businesses that have the technological expertise in furthering the mission of NIH, particularly in areas dealing with diagnostic problems in the elderly, the development of new prostheses, and other issues involving health care delivery. One example is a grant that deals with the development of a video medication education program for senior citizens which addresses the problems of multiple medications among the elderly.

CONTRACTS

Mr. Early. Would you give us a few examples of how the Institute utilizes its Research & Development contract mechanisms?

Dr. Williams. The NIA uses research and development contracts for three major purposes. About 28% of contract dollars support research resources. These include cellular and genetic study resources and vertebrate models such as rats, mice, and nonhuman primates. These resources are available to any NIA-supported researcher who may have need of them. Another 33% is devoted to epidemiological research, including the four large NIA population contracts and two epidemiological studies on Alzheimer disease. The final major use, accounting for about 34% of the funds, is support of the clinical trials on systolic hypertension in the elderly.

Mr. Early. Under your FY 1987 request you will be supporting only 42 R&D contracts, as compared to the FY 1986 post-sequestration level of 46. What impact will it have on your research initiatives?

Dr. Williams. All major on-going contracts scheduled for continuation in FY 1987 will be funded at or near current levels. The NIA is also considering a variety of contracts for future funding on topics such as hip fracture, behavioral treatment of elevated blood pressure in the elderly, and a pathology evaluation of the Wistar rat. Another initiative of particular concern which may be delayed is a planned contract to develop guidelines for updating the U.S. Recommended Dietary Allowances (RDAs) to take into account the nutritional needs of older people. The contract would amount to $100,000 per annum for 3 years. Despite growing evidence that nutritional requirements may change with age throughout the later years and may have great effects on health, the current RDAs do not reflect this.

Mr. Early. What effect does this "unstableness" have on your programs?

Dr. Williams. While ongoing research supported by contract can be maintained at approximately FY 1986 levels, the reduced levels effectively preclude new contracts focused on new initiatives. In addition, planned expansion of some contracts -- such as the addition of clinical studies to the four major epidemiological population studies -- may have to be postponed indefinitely.

TEACHING NURSING HOMES

Mr. Early. According to the justification you are supporting seven teaching nursing homes. Doctor, haven't you indicated in the past that you would probably be adding another teaching nursing home? Have budget constraints been the reason for not expanding this program?

Dr. Williams. We have indicated our desire to expand the Teaching Nursing Home (TNH) program to as many as twelve projects. However, we will not be able to expand the program this fiscal year. We believe an expansion of the program to a minimum of eight projects in FY 1987 would be worthwhile.

Mr. Early. Do you have any plans to expand this program in FY 1987?

Dr. Williams. We do not anticipate any expansion at this time. The first two TNHs, funded in FY 1982, are expected to submit competing renewal applications in FY 1987. Because of limitations in the proposed FY 1987 budget, it is likely that we will only be able to fund one of these renewal applications.

Mr. Early. Who are the recipients of the teaching nursing home project grants? For the record would you please provide a short description of the main projects each is supporting.

Dr. Williams. The following is a list of TNH research projects, with some highlights of particularly important findings:

Albert Einstein College of Medicine, New York, New York
Principal Investigator: Leslie Wolfson, M.D.
Project I: Dementias
Project II: Osteoarthritis-Synovial Cell-Cartilage Interaction
Project III: Falls in the Elderly
Project IV: Cognitive and Genetic Aspects of Alzheimer's

The research project "Falls in the Elderly" has found that some older people suffer drastic losses in strength in specific leg muscles and/or lose accurate sensation of leg position and that these people are at markedly increased risk of falling. The identification of such specific factors may eventually lead to effective ways of preventing falls by reversing or compensating for these dysfunctions.

Philadelphia Geriatric Center, Philadelphia, Pennsylvania
Principal Investigator: Donald Kaye, M.D.
Project I: Urinary Tract Infections in a Geriatric Population
Project II: Cognitive Rehabilitation of Stroke
Project III: Regional Metabolism and Flow in Aging and Dementia
Project IV: Modification of Exercise Capacity in the Elderly
Project V: Sleep Apnea Syndrome in the Elderly

The prevalence of urinary tract infections increases markedly with age. The project, "Urinary Tract Infections in a Geriatric Population" has found that bacteria which cause urinary tract infections adhere in greater numbers to urinary tract cells of older men than of younger men. This may contribute to the increased risk of among older men. This finding may be useful in the future for developing new ways of preventing these infections.

Case Western Reserve University, Cleveland, Ohio
Principal Investigator; Amasa Ford, M.D.
Project I: Cleveland GAO Study of the Elderly: A Follow-up
Project II: Performance and Control of the Respiratory Muscles
Project III: Autonomic and Airway Reactivity in the Aged

Research at Case Western Reserve University is involved in studying respiratory function in the elderly. Impaired respiration is involved in sleep apnea, a common condition among the elderly, in which breathing ceases for brief periods during sleep. This condition places subjects at increased risk of mortality. Sleep apnea appears to be related to decreased respiratory muscle strength, and researchers on this project have found that such age-related decreases can be reversed by training programs.

Hebrew Rehabilitation Center for Aged, Boston, Massachusetts
Principal Investigator: John Rowe, M.D.
Project I: Syncope and Blood Pressure Homeostatis in the Elderly
Project II: Bladder Function and Incontinence in the Frail Elderly
Project III: Vitamin D Nutrition in the Institutionalized Elderly
Project IV: Identification of Persons at Risk of Institutional Placement
Project V: Clinical and Neuroendocrine Measures of Depression in SDAT
Project VI: Vasopressin Release in Dementia

Recent studies at the Hebrew Rehabilitation Center for Aged indicate that reductions in blood pressure following meals may be an important cause of syncope (fainting) among the elderly. It has been found that while younger people had no reduction in blood pressure after a meal, systolic blood pressure in older people without previous episodes of syncope dropped an average of 22mm Hg, and dropped by an average of 34mm Hg in older people with a history of falls. These findings suggest that there may be age-associated impairments in neuroendocrine regulation of blood pressure, which in some cases are severe enough to cause syncope.

The Johns Hopkins Hospital, Baltimore, Maryland
Principal Investigator: William Hazzard, M.D.
Project I: The Effect of Training on Exercise Function During Aging
Project II: Aging, Adiposity, Physical Fitness and Endocrine - Metabolic Function
Project III: Aging, Adiposity and Sleep Disordered Breathing
Project IV: Neurobehavioral Performance in Aging and the Role of Sleep Disordered Breathing

Though the prevalence of sleep apnea increases markedly with age, these findings indicate that obesity-related factors rather than age itself may be a major risk factor for sleep apnea in older people. Research at the Johns Hopkins Hospital have also found that placing obese elderly sleep apnea patients on a weight-reducing diet lowers the frequency of sleep apnea. Interestingly, this effect occurred before any significant reduction in weight. Preliminary findings suggest that this may be due to changes in carbohydrate metabolism, and that carbohydrate loading may be a previously unappreciated contributor to sleep apnea that is reversible by dietary control.

University of California, San Diego, La Jolla, California
Principal Investigator: Elizabeth Barrett-Connor, M.D.
Project I: Epidemiology of Nosocomial Infections
Project II: Effects of Hypnotics on Sleep Apnea
Project III: Predictors of Institutionalization in the Adult Community

The project "Effects of Hypnotics on Sleep Apnea" investigates the effects of hypnotic medication (commonly used "sleeping pills") on sleep apnea. There is current evidence that hypnotic medications increase the number of apneas during sleep. Mortality from all causes rises about 30% during the hours of sleep, and it is possible that sleep apnea is at least a contributing factor in some nocturnal deaths which are attributed to heart disease or cerebrovascular accidents. The interactions between hypnotics and apnea may be a crucial factor in a certain number of these nocturnal deaths. This project has also found an association between sleep apnea and dementia.

Stanford University School of Medicine, Stanford, California
Principal Investigator: Gerald Reaven, M.D.
Project I: Disturbed Sleep and Daytime Alertness in the Nursing Home
Project II: Age Related Changes in Parathyroid Function in Humans
Project III: Type II (NIDDM) Diabetes and Renal and Cognitive Function in Older Patients
Project IV: Psychological Treatments of Memory Deficits in Nursing Homes

Studies at Stanford are teaching nursing home patients to use mnemonic (memorization) techniques to remember such things as names and daily routines. While simple memory training procedures have been around for some time, this will be the first time scientists are systematically attempting to train nursing home patients and to follow those patients over time to see if they continue to use the procedures.

Mr. Early. What is the average size of the teaching nursing home project grant award for FY 1986? What will they be in FY 1987?

Dr. Williams. The average cost of a teaching nursing home in FY 1986 will be about $686,000. The average cost in FY 1987 will be approximately $650,000.

GERIATRIC LEADERSHIP ACADEMIC AWARDS

Mr. Early. How many Geriatric Leadership Academic Awards were made in FY 1986, and who were the grant recipients? Was FY 1985 the first year these awards were made?

Dr. Williams. FY 1985 was the first year the Geriatric Leadership Academic Awards were made. Two were awarded: one to Jerome Kowal at Case Western Reserve University and the second to Jeffrey B. Halter, at the University of Michigan/Ann Arbor. To date, we have received 8 applications in FY 1986. These have not yet gone through the peer review process, but we would expect at least one or two to be within the fundable range.

Mr. Early. How many Geriatric Leadership Awards will be made in FY 1987?

Dr. Williams. At the moment, we are projecting one additional Geriatric Leadership Award in FY 1986.

CO-FUNDED TRAINEES

Mr. Early. How many trainees will be supported under co-funded awards in FY 1986? How many will be supported in FY 1987?

Dr. Williams. Eleven of the trainees co-funded in FY 1985 will also be supported in FY 1986. Three will continue into FY 1987. Currently, given the limited number of competing FTTPs available in both FY 1986 and FY 1987, it is uncertain how many additional co-funded trainees will receive awards in these years.

MULTI-INFARCT DISEASE

Mr. Early. The justification mentions that if the finding of white matter lesions is an early indication of multi-infarct disease, then diet and life style change may prevent further damage. Would you elaborate on what sort of diet and life style changes you are referring to.

Dr. Williams. Isolated Systolic Hypertension (ISH) is a form of hypertension almost uniquely confined to persons over 60 years of age. In addition to major strokes resulting in death or paralysis, ISH is a cause of repeated small strokes which often lead to multi-infarct dementia. Preventing ISH would, therefore, have a definite impact on the incidence of multi-infarct dementia.

Many studies of populations around the world show wide variation in the tendency for blood pressure to increase with age, and some population groups are completely free of it. The studies suggest that differences in diet and life style may determine blood pressure trends with age. Research is currently focusing on various forms of vegetarian diets, the low sodium-high potassium combination found in some relatively stroke-free populations, high polyunsaturated-to-saturated fat ratios, and studies of calcium intake.

RESEARCH PRIORITIES

Mr. Early. If an increase over the FY 1987 request is provided, how would you use these additional funds?

Dr. Williams. We would use these funds to support research programs of highest priority to the NIA. These include molecular genetics, Alzheimer disease, the oldest old, osteoporosis, and training. Each of these areas has the potential to significantly enhance the health and effective functioning of older individuals. Molecular genetics overlaps many areas of research and provides new opportunities to answer questions which previously were unanswerable. Alzheimer disease creates devastating psychological, social, and financial burdens. The oldest old are the fastest growing segment of the nation's population. Osteoporosis is directly related to hip fractures, a major cause of disability among older people. Training enough researchers and academicians in the fields of geriatrics and gerontology is essential to assure adequate medical and support services for the future older population.

Training of researchers and academicians in the field of aging continues to be a top priority. The need for greatly increased numbers of trained individuals is clearly defined in the HHS Task Force Report, which recommended a doubling to tripling of the yearly numbers of postdoctoral fellows and trainees in order to reach minimally adequate numbers of faculty in the Nation's medical and other health professional schools by the year 2000.

LOST RESEARCH INITIATIVES OR OPPORTUNITIES

Mr. Early. Will any significant new research initiatives or opportunities be lost or delayed by lack of funds in the FY 1987 budget? Please provide for the record a list of these, along with a brief description and the funding requirements associated with each.

Dr. Williams. The Alzheimer Disease Research Centers have several important projects which will be unfunded or funded at reduced levels. Examples include:

1) A project to identify DNA pieces carrying the gene for familial AD
2) Recruitment f patients with AD for study at the Alzheimer Disease Research Centers (ADRC)
3) Development of a core facility for molecular biological studies at one of the ADRCs
4) Autopsies on brain samples from proven AD patients
5) Funding for a conference on neural transplants, a potential treatment for AD

To support these projects and fully fund the Alzheimer Disease Research Centers would require an additional $2.3 million.

The NIA has been considering implementation of a program of research related to the international epidemiology of Alzheimer disease (AD) and related disorders, and to the influence of race and ethnicity on AD in the United States. This interest is based on preliminary information which has suggested that there may be major differences in the occurrence of AD in different countries and in different ethnic groups. The comparison of rates of dementia in Americans of differing race and ethnicity offers the opportunity to examine genetic and cultural factors in the development of these diseases. The planned activities would cost approximately $400,000 in FY 1987, increasing to approximately $1.2 million per year for the ensuing five years.

The NIA has planned an initiative in cooperation with the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) for FY 1987. The initiative will fund comprehensive research programs on the causes, prevention, and treatment of osteoporosis at academic medical centers. It is titled "Programs of Excellence of Research on Osteoporosis." In view of budgetary constraints, NIA will be able to fund only 2 Programs of Excellence of Research on Osteoporosis for an estimated total cost of $2.25 million in FY 1987. The magnitude of the public health problem and the readiness of the scientific community warrant the funding of at least four additional programs in FY 1987 for an additional $4.5 million.

The Laboratory of Molecular Genetics (LMG) began operations in October 1985. The LMG has been successful in attracting two very talented young researchers to join its staff. The initial goal had been to attract four independent scientists as the core of this new laboratory. In response to reductions in FTE ceilings, recruiting has been reduced by 25% and only one additional independent scientist is being recruited. In response to sequestration, the budget of this laboratory has been reduced to $330,000. To bring the staffing levels of LMG to initial staffing projections would require an additional four FTE's and to reach initial plans for equipping this laboratory would require an additional $500,000 in FY 1987.

Extramural investigators interested in the biology of aging are also beginning to employ recombinant DNA technology in the study of genes related to aging processes and to specific problems such as familial Alzheimer disease. The NIA has issued a program announcement soliciting research applications in this area. It was anticipated to fund at least ten new projects in this area totaling $2.0 million dollars in FY 1987, but it now appears that only two or three projects will be funded for about $300,000.

An area of postponed emphasis will be a new research initiative on neuroendocrine factors in the aging immune system. This is an effort to study brain-immune system interactions in the aging organism. Although there is much current interest in detailing how emotions and cognitive states influence the immune system through the brain and neuroendocrine systems, there are few studies that directly address the interaction of these systems with older people. By better understanding how behavior influences immunologic functioning, new treatment modalities can be developed to supplement current pharmacologic approaches to immune-mediated diseases of older people, such as arthritis and autoimmune disorders. The next 5 to 10 years have the potential of seeing exciting and significant developments in this area if funding can be used to support at least 5 grants per year at a cost of about $500,000 per year.

NIA intramural staff have designed an international study to answer whether specific age-related heart changes which occur within our "normal" range are in fact "normal" or whether they are absent in a population in which blood pressure does not increase with age. Vascular stiffness and left ventricular wall thickness and filling properties would be measured in a large number of individuals in two populations of the People's Republic of China: one that exhibits an age-related increase in blood pressure with age; and one in which this increase does not occur or is retarded. This study would require $200,000 in FY 1987.

Another initiative focuses on nutrition of older people. It includes a Request for Applications for a Special Emphasis Research Career Award (SERCA) for training and research support of scientists seeking careers in nutritional and metabolic factors in aging. Research on nutrition for older people and the cadre of appropriately trained scientists to carry out such research is very inadequate. We estimate a need for at least 10 such awards in FY 1987, which would require $0.6 million. Because of budget constraints, we believe we will be able to make 2 such award in FY 1987. NIA has also planned support for a 3-year contract amounting to $100,000 per annum to develop guidelines for updating the U.S. Recommended Dietary Allowances (RDAs) to take into account the nutritional needs of older people. Without additional funds in NIA's contracts budget, it is unlikely that we will be able to support this effort.

Since 1982, the NIA has been collecting data on health conditions and disabilities of approximately 10,000 people 65 and over in three locations, and have continued collecting information on change in health status on the same individuals since that time. A fourth location was established in 1984 and is currently collecting baseline information on approximately 3800 participants, giving a total of 13,800 older people under study. The data collected has provided information on history of disease, disabilities and impairments, nursing home episodes and hospitalizations. There is a need for clinical information on these representative samples of older people living in communities. Little is known at present about the anatomy, physiology, and functioning of healthy, noninstitutionalized older people, factors associated with good health in later life, and pathways of health decline which precede mortality and loss of independence. This proposed research would cost approximately $750,000 per year for each of the four population studies for a total of $3,000,000.

REDUCTIONS IN RESEARCH

Mr. Early. Doctor, will any significant research initiative currently underway be halted or seriously delayed due to FY 1987 funding levels?

Dr. Williams. High priority research initiatives, such as Alzheimer disease, molecular genetics, osteoporosis, and the oldest old, will be funded at or near the FY 1986 levels. They will be affected primarily by an inability to expand the level of research support to take advantage of new opportunities. The Alzheimer Disease Research Centers will also be affected by continued support at less than the fully recommended levels.

Mr. Early. To what extent will there be major reductions in the scope of ongoing or new initiatives because of the FY 1987 funding levels? For the record, provide a list of these along with a brief description and the amounts associated with each initiative.

Dr. Williams. The 10 NIA Alzheimer Disease Research Centers have never been funded at the full recommended level. The ADRC directors have used a variety of methods to minimize the effects of these short-falls, including delaying the hiring of personnel essential to some projects, delaying the purchase of some equipment, postponing the start of some projects, and/or reducing the number of patients being studied or recruited for the clinical studies. To fund these centers at the full recommended level would require approximately an additional $2.3 million in FY 1987.

NIA efforts in the areas of falls and osteoporosis are limited by the current budgetary restraints. The NIA anticipates funding approximately 6 to 8 investigations on falls for a total cost of $1.25 million in FY 1986. Establishment of a core of investigations on falls would require an additional 6 to 8 studies in Fy 1987 and a doubling of available funds to $2.5 million.

For the oldest old, opportunities exist at the Bureau of the Census to produce a special data file from the Current Population Survey that will allow for (a) the first study of trends in the poverty status among the very old including the relation to health; (b) producing tabulations from the Survey on Income and Program Participation as well as supplementing the inadequate numbers of the very old in the Survey; (c) expanding the health and living arrangements components of the International Database on Aging; and (d) for creation of a data base on the foreign-born older population.

At the National Center for Health Statistics, opportunities exist (a) to extend the Longitudinal Study on Aging in order to assess the important transitions that occur between dependence and the return to full or partial independent functioning and living, (b) to plan for a new Supplement on Aging concentrated on the very old and including physical examinations of functioning in everyday life, and (c) to extend the historic data file on the Health Interview Survey to include hospital discharges. In the areas outlined above -- data bases, individual research grants and workshops, and epidemiological studies -- would require approximately $3.2 million in additional funds in FY 1987.

The 1984 Report of the Health and Human Services (HHS) Task Force on Geriatrics and Gerontology, documented the need for many more research investigators and educators in these fields. Among other recommendations, the plan calls for a doubling to tripling of the yearly numbers of postdoctoral fellows and trainees in order to reach minimally adequate numbers of faculty in the Nation's medical and other health professional schools by the year 2000. In response to this need, the NIA has intensified its efforts to train investigators and educators in aging research. The number of competing NIA extramural and intramural training positions rose from 57 in FY 1980 to 106 in FY 1985. However, according to the FY 1986 revised budget, NIA expects to be able to fund 48 new trainees in FY 1986. The President's FY 1987 Budget provides for 53 competing extramural and intramural trainees. At the reduced rate, Objective Five of the HHS Report on Education and Training in Geriatrics and Gerontology, calling for at least 600 investigators -- other than physicians -- to be prepared by 1990, and 1,300 by 2000, will not be met.

An additional $2.7 million would support 79 more new trainees, bringing the number of new trainees in FY 1987 to 132, and the total number of intramural and extramural trainees to approximately 377. Of this amount, $1.1 million would be for research career awards and $1.4 million for individual fellowships and institutional awards. Another $200,000 would support additional intramural staff fellows.

Intramural research will also be affected by the FY 1987 funding levels. Selected aspects of the Baltimore Longitudinal Study of Aging (BLSA) will be curtailed or delayed. Replacement of participants, lost through death or as dropouts, and recruitment of women will be slowed. Plans to have longitudinal analyses of selected BLSA data sets (e.g., pulmonary function, history and physical, hearing, motor skills) performed via contract must be deferred. As numerous investigators rely on central data sets, the unavailability of such analyses has a ripple effect and undercuts the multidisciplinary aspect of the BLSA which is one of the study's chief assets. Other BLSA areas which warrant increased emphasis but cannot be pursued in FY 1987 include: follow-on studies to capitalize on promising research results and the introduction of new technologies; research on antecedents of frailty in healthy people; study of the overall characteristics of successful aging drawing upon accumulating BLSA data; and use of the BLSA as a source of research experience for physicians in academic medicine who have clinical training in geriatrics but lack the research background necessary to their career advancement. Full utilization of the BLSA would require an additional $500,000.

Two other areas of intramural research are also of particular concern: full implementation of the recently established Laboratory of Molecular Genetics and further development of the Laboratory of Neurosciences. The high priority Laboratory of Molecular Genetics has begun to investigate the molecular basis for aging and age-dependent diseases. One collaborative project with the NIA intramural Clinical Immunology Section is examining the molecular basis for the decline in immune function that occurs with human aging, looking specifically at the expression of the interleukin II gene; another involves the study of genes that may be related to Alzheimer's disease. At present funding levels, development of an intramural capability to employ recombinant DNA techniques in the study of genes related to aging processes will be slowed. Additional resources needed to implement initial plans for the Laboratory's development include $500,000 in FY 1987.

The NIA Laboratory of Neurosciences (LNS) is contributing important new insights in elucidating brain processes in healthy aging and in Alzheimer disease. A combination of sophisticated new techniques is being used to examine fundamental brain processes in three populations: healthy subjects of different ages; Alzheimer disease; and Down syndrome. Several important new initiatives will be slowed or deferred at current funding levels. These include: initiation of a clinical neuropathology and neurochemistry program to correlate *in vivo* findings with brain pathology and neurochemistry *post mortem*; emphasis on applied mathematical biology and computerized approaches to data analysis and image processing to enhance their sensitivity for purposes of diagnostic accuracy; studies of pharmacokinetics and pharmacodynamics of central nervous system drugs; and a medical genetics focus to look for specific biological markers and evaluate the possible role of genetic factor in the LNS patient populations. Additional resources required to support these activities include $1,130,000.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

National Institute on Aging

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NATIONAL INSTITUTES OF HEALTH

National Institute on Aging

For carrying out section 301 and title IV of the Public Health Service Act with respect to aging, [$156,592,000] *$145,829,000 (Department of Health and Human Services Appropriation Act, 1986.)*

NATIONAL INSTITUTES OF HEALTH

National Institute on Aging

Amounts Available for Obligation 1/

	1985 Actual	1986 Appropriation 1/	1987 Estimate
Appropriation	$144,521,000	$156,592,000	$145,829,000
Enacted administrative reduction	--	-101,000	--
Sequester order	--	-6,729,000	--
Proposed rescission	--	-2,679,000	--
Subtotal, adjusted appropriation	144,521,000	147,083,000	145,829,000
Comparative transfer from: National Institute of Mental Health for changes in the central services financing mechanisms and formulas	341,000	--	--
Subtotal, adjusted budget authority	144,862,000	147,083,000	145,829,000
Unobligated balance, start of year	--	1,323,000	--
Unobligated balance, end of year	-1,323,000	--	--
Unobligated balance, lapsing	-230,000	-139,000	--
Total obligations	143,309,000	148,267,000	145,829,000

1/ Excludes the following amounts for reimbursable activities carried out by this account: 1985 -- $320,000; 1986 -- $819,000; 1987 -- $819,000.

National Institute on Aging

Budget Mechanism

(Dollars in Thousands)

	1986 1/ Appropriation		1986 Available 1/ after 2/ Sequestering		1986 1/ Revised 2/		1987 Estimate	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research Grants:								
Research Projects:								
Noncompeting	303	60,130	303	57,544	303	57,544	345	60,618
Admin. supplementals	(8)	128	(8)	123	(8)	123	(8)	128
Competing								
Renewal	45	7,992	45	7,408	45	7,408	33	5,066
New	151	24,290	151	23,536	129	20,885	109	18,282
Supplemental	5	160	5	160	3	132	3	154
Subtotal, competing	201	32,442	201	31,104	177	28,425	145	23,502
Subtotal, research projects	504	92,700	504	88,771	480	86,092	490	84,248
Research Centers								
Specialized/comprehensive ctrs.	12	10,396	12	9,949	12	9,949	12	9,812
Subtotal, research centers	12	10,396	12	9,949	12	9,949	12	9,812
Other Research:								
Research Career Programs	71	4,759	70	4,554	70	4,554	68	4,512
Minority biomed. res. support	(6)	373	(5)	357	(5)	357	(5)	307
Other research related	14	1,079	11	1,033	11	1,033	10	829
Subtotal, other research	85	6,211	81	5,944	81	5,944	78	5,648
Total, Research Grants	601	109,307	597	104,664	573	101,985	580	99,708

Training								
Individual awards								
Noncompeting	21	494	21	494	21	494	22	519
Competing								
Renewal								
New	12	288	11	254	11	254	8	194
Subtotal, individual	33	782	32	748	32	748	30	713
Institutional								
Noncompeting	174	3,954	174	3,954	174	3,954	132	3,590
Competing								
Renewal	14	332	9	209	9	209	11	256
New	19	439	15	359	15	359	22	550
Subtotal, institutional	207	4,725	198	4,522	198	4,522	165	4,396
Total, Training	240	5,507	230	5,270	230	5,270	195	5,109
Research & Development Contracts	48	13,733	46	13,142	46	13,142	42	12,590
					FTEs		FTEs	
Intramural Research		20,915		19,986	245	19,986	245	20,250
Research Management and Support		8,352		7,884	95	7,884	95	8,172
Disease Control								
Construction								
Total, NIA		157,814		150,946	340	148,267	340	145,829

1/ Reflects an administrative reduction of $101,000 and a carryover in unobligated funds of $1,323,000.

2/ Reflects a consultant services (Section 515 of the Treasury-Postal Service Appropriation Act, 1985) witholding of $139,000.

NATIONAL INSTITUTES OF HEALTH

National Institute on Aging

CROSSWALK - 1986 Appropriation 1/

(Dollars in thousands)

PROGRAM ACTIVITY	Research Grants			Training Programs		Research and Devel. Contracts	Intramural Research	Res. Mgmt. and Support	Total
	Research Projects	Research Centers	Other Research	Indiv.	Instit.				
Aging................	$92,700	$10,396	$6,211	$782	$4,725	$13,733			$128,547
Intramural research.							$20,915		20,915
Research management and support.......								$8,352	8,352
Total...............	92,700	10,396	6,211	782	4,725	13,733	20,915	8,352	157,814

1/ Reflects an administrative reduction of $101,000 and a carryover in unobligated funds of $1,323,000.

National Institute on Aging

CROSSWALK - 1986 Available after Sequestering 1/ 2/

(Dollars in thousands)

PROGRAM ACTIVITY	Research Grants			Training Programs		Research and Devel. Contracts	Intramural Research	Res. Mgmt. and Support	Total
	Research Projects	Research Centers	Other Research	Indiv.	Instit.				
Aging...............	$88,771	$9,949	$5,944	$748	$4,522	$13,142			$123,076
Intramural research.							$19,986		19,986
Research management and support.......								$7,884	7,884
Total...............	88,771	9,949	5,944	748	4,522	13,142	19,986	7,884	150,946

1/ Reflects an administrative reduction of $101,000 and a carryover in unobligated funds of $1,323,000.

2/ Reflects a consultant services (Section 515 of the Treasury-Postal Services Appropriation Act, 1986) withholding of $139,000.

NATIONAL INSTITUTES OF HEALTH

National Institute on Aging

CROSSWALK - 1986 Revised Estimate 1/ 2/

(Dollars in thousands)

PROGRAM ACTIVITY	Research Grants			Training Programs		Research and Devel. Contracts	Intramural Research	Res. Mgmt. and Support	Total
	Research Projects	Research Centers	Other Research	Indiv.	Instit.				
Aging...............	$86,092	$9,949	$5,944	$748	$4,522	$13,142			$120,397
Intramural research.							$19,986		19,986
Research management and support.......								$7,884	7,884
Total...............	86,092	9,949	5,944	748	4,522	13,142	19,986	7,884	148,267

1/ Reflects an administrative reduction of $101,000 and a carryover in unobligated funds of $1,323,000.

2/ Reflects a consultant services (Section 515 of the Treasury-Postal Services Appropriation Act, 1986) withholding of $139,000.

NATIONAL INSTITUTES OF HEALTH

National Institute on Aging

CROSSWALK - 1987 Congressional Justification

(Dollars in thousands)

PROGRAM ACTIVITY	Research Grants			Training Programs		Research and Devel. Contracts	Intramural Research	Res. Mgmt. and Support	Total
	Research Projects	Research Centers	Other Research	Indiv.	Instit.				
Aging...............	$84,248	$9,812	$5,648	$713	$4,396	$12,590			$117,407
Intramural research.							$20,250		20,250
Research management and support.......								$8,172	8,172
Total...............	84,248	9,812	5,648	713	4,396	12,590	20,250	8,172	145,829

National Institute on Aging

Summary of Changes

1986 Revised estimate	$148,267,000
1987 Estimated obligations	145,829,000
Net change	-2,438,000

	1986 Base Amount	Change from Base Amount
Increases:		
A. Built-in:		
1. Within grade increase	$11,831,000	+$204,000
2. Federal Employees Compensation Fund increase	59,000	+11,000
3. FTS rate increase	118,000	+32,000
4. Service and Supply Fund increase	2,852,000	+120,000
5. Gerontology Research Center maintenance contract	3,053,000	+128,000
6. Increased cost of laboratory supplies, materials and other expenses	8,467,000	+355,000
Subtotal		+850,000
B. Program:		
1. Research Projects		
a. Noncompeting continuations converting from competing status	57,667,000	+26,953,000
b. Competing (new, renewals and supplementals)	28,425,000	+23,502,000
2. Centers		
a. Noncompeting continuations converting from competing status	8,946,000	+1,003,000
b. Competing (new, renewals and supplementals)	1,003,000	+226,000
3. Other Research Research Career Program		
a. Noncompeting continuations converting from competing status	4,092,000	+481,000
b. Competing completed or converting to noncompeting status	462,000	+500,000
Other		
a. Noncompeting contiuations	971,000	+133,000
b. Competing (new, renewals and supplementals)	419,000	+186,000

Summary of Changes - continued

	1986 Base Amount	Change from Base Amount
4. Individual Training		
a. Noncompeting continuations converting from competing status	494,000	+254,000
b. Competing (new, renewals and supplementals)...............	254,000	+194,000
5. Institutional Training		
a. Noncompeting continuations converting from competing status	3,954,000	+592,000
b. Competing (new, renewals and supplementals)...............	568,000	+806,000
6. Intramural Research: program increases in high priority areas	—	+246,000
Subtotal..................	—	+55,076,000
Total, Increases..........................	—	+55,926,000
Decreases:		
A. Built in:		
1. Payment for centrally furnished services..........................	4,062,000	-544,000
Subtotal.................	—	-544,000
B. Program:		
1. Research Projects		
a. Noncompeting completed or converting to competing status	57,667,000	-23,874,000
b. Competing completed or converting to noncompeting status.......................	28,425,000	-28,425,000
2. Centers		
a. Noncompeting completed or converting to competing status.........................	8,946,000	-363,000
b. Competing completed or converting to noncompeting status.........................	1,003,000	-1,003,000
3. Other Research Research Career Program		
a. Noncompeting completed or converting to competing status	4,092,000	-561,000
b. Competing completed or converting to noncompeting status........................	462,000	-462,000

Summary of Changes - continued

	1986 Base Amount	Change from Base Amount
Other		
a. Noncompeting completed or converting to competing status	971,000	-154,000
b. Competing (new, renewals and supplementals)	419,000	-419,000
4. Individual Training		
a. Noncompeting completed or converting to competing status	494,000	-229,000
b. Competing completed or converting to noncompeting status	254,000	-254,000
5. Institutional Training		
a. Noncompeting completed or converting to competing status	3,954,000	-956,000
b. Competing completed or converting to noncompeting status	568,000	-568,000
6. Research and development contracts	13,142,000	-552,000
Subtotal	—	-57,820,000
Total, decreases	—	-58,364,000
Total, net change	—	-2.438,000

National Institute on Aging

Budget Authority by Activity

(Dollars in thousands)

	1986 Appropriation	1986 Available after sequestering	1986 Revised		1987 Estimate	
	Amount	Amount	FTEs	Amount	FTEs	Amount
Aging..............	128,547	123,076	--	120,397	--	117,407
Intramural research..........	20,915	19,986	245	19,986	245	20,250
Research management and support........	8,352	7,884	95	7,884	95	8,172
Total..........	157,814	150,946	340	148,267	340	145,829
Unobligated balance, start of year......	-1,323	-1,323		-1,323		--
Unobligated balance, lapsing...........	--	139		139		--
Total......	156,491	149,762		147,083		145,829

NOTE: All 1986 columns reflect a consultant services (Section 515 of the Treasury-Postal Service Appropriation Act, 1985) withholding of $139,000; an enacted administrative reduction of $101,000; and a carryover in unobligate funds of $1,323,000.

National Institute on Aging

Obligations by Object

	1985 Actual	1986 Estimate	1987 Estimate
Total number of full-time permanent positions..........................	304	304	304
Total compensable workyears:			
Full-time equivalent employment.....	380	368	368
Full-time equivalent of overtime and holiday hours..................	3	3	3
Average ES salary......................	$66,920	$66,920	$66,920
Average GS grade.......................	9.14	9.14	9.14
Average GS salary......................	$28,224	$28,224	$28,224
Average salary, grades established by act of July 1, 1944 (42 U.S.C.207)..	35,361	35,361	35,361
Average salary of ungraded positions..	23,206	23,206	23,206
Personnel compensation:			
Permanent positions..................	7,966,000	7,998,000	8,117,000
Positions other than permanent.......	2,982,000	2,993,000	3,038,000
Other personnel compensation.........	350,000	343,000	348,000
Special personnel services payments..	497,000	497,000	504,000
Subtotal, personnel compensation...	11,795,000	11,831,000	12,007,000
Personnel benefits....................	1,588,000	1,596,000	1,616,000
Benefits for former personnel.........	22,000	22,000	22,000
Travel and transportation of persons..	349,000	349,000	364,000
Transportation of things..............	72,000	72,000	72,00

	1985 Actual	1986 Estimate	1987 Estimate
Rent, communications, and utilities...	1,061,000	1,106,000	1,152,000
Printing and reproduction............	365,000	365,000	365,000
Other Services:			
Project contracts....................	11,557,000	13,142,000	12,590,000
Payment for centrally furnished servi	3,596,000	4,014,000	3,467,000
Standard level user charge...........	327,000	48,000	51,000
Other................................	5,662,000	4,701,000	5,354,000
Supplies and materials...............	2,080,000	1,872,000	1,965,000
Equipment............................	2,105,000	1,894,000	1,987,000
Grants, subsidies, and contributions..	102,730,000	107,255,000	104,817,000
Total................................	143,309,000	148,267,000	145,829,000

National Institute on Aging
Significant Items in House Appropriation Committee Reports

Item	Action taken or to be taken
1986 House Report	
1. "The Committee also expects that the Department will continue to call upon its interagency committee on geriatric training to work toward easing the current shortage of medical and health personnel trained in aging issues." (p. 72)	1. The DHHS interagency committee on geriatric training has continued to meet throughout this past year. Information on the progress of member agencies is exchanged on a regular basis, and efforts are being made to encourage more training in the field of geriatrics.

National Institute on Aging Significant Items Senate Appropriation Committee Reports

Item	Action taken or to be taken
1986 Senate Report	
1. "The Committee strongly encourages the Institute to continue its training efforts in these areas. The Committee also expects the Department to keep its interagency committee on geriatric training actively involved in easing the current shortage of medical and health personnel trained in aging research." (pp. 100-101)	1. The NIA continues to participate in the meetings of the DHHS committee on geriatric training, which has met regularly throughout the past year. The NIA is also currently collaborating with the Health Resources and Services Administration on a second conference in geriatric education, to be held in June 1986.

NATIONAL INSTITUTES OF HEALTH
National Institute on Aging

Authorizing Legislation

	PHS Act/ Other Citation	U.S. Code Citation	1986 Amt. Authorized	1986 Estimate	1987 Amt. Authorized	1987 Budget Estimate
Research and Investigation.....	Section 301	42§241	Indefinite	$142,997,000	Indefinite	$140,720,000
National Institute on Aging....	Title IV Part H	42§289k-2 - 289k-5	Indefinite		Indefinite	
onal Research Service Awards	Section 487	42§288	$244,000,000[1]	5,270,000	$260,000,000[1]	5,109,000
Total Budget Authority........				148,267,000		145,829,000

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[1] This training authority is shared with other research training programs of the National Institutes of Health; the Alcohol, Drug Abuse and Mental Health Administration and the Health Resources and Services Administration.

National Institute on Aging

Appropriations History

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation 1/
1978......	34,838,000	39,305,000	35,305,000	37,305,000
1979......	37,910,000	54,526,000	49,500,000	56,911,000
1980......	56,738,000	68,910,000	70,000,000	69,988,000
1981......	74,441,000	75,493,000	75,469,000	75,608,000
1982......	74,084,000 2/	86,059,000	85,591,000	81,903,000
1983......	84,556,000	96,104,000	91,887,000	93,993,000
1984......	99,408,000	112,516,000 3/	112,084,000 3/	115,720,000
1985......	117,390,000	140,102,000 4/	144,799,000	144,862,000
1985 Proposed Rescission..	-195,000			
1986......	135,376,000	149,067,000 5/	156,618,000	156,491,000
1986 Sequester....	-6,729,000			
1986 Proposed Rescission...	-2,679,000			
1987......	145,829,000			

1/ Reflects enacted supplementals, rescissions, and reappropriations.

2/ Reflects the September Amendment; the original request was $84,186,000.

3/ Excludes $2,168,000 in NRSA training programs not considered.

4/ Excludes $3,069,000 in NRSA training programs not considered.

5/ Excludes $4,642,000 in NRSA training programs not considered.

National Institute on Aging

Justification
(Dollars in Thousands)

	1986 Appropriation Amount	1986 Available after Sequestering Amount	1987 Revised FTEs	1987 Revised Amount	1987 Estimate FTEs	1987 Estimate Amount
Aging.........	$128,547,000	$123,076,000	—	$120,397,000	—	$117,407,000
Intramural research......	20,915,000	19,986,000	245	19,986,000	245	20,250,000
Research management and support...	8,352,000	7,884,000	95	7,884,000	95	8,172,000
Total.........	157,814,000	150,946,000	340	148,267,000	340	145,829,000

General Statement

At the present time, approximately 12% of the United States population is aged 65 or above. This figure is expected to rise to 20% by the year 2030. Among those aged 65 and above, the fastest growing group is those over 85. The 85 plus age group has been growing at almost three times the rate for all other persons over age 65. The overall increase, and especially the increased numbers of the oldest old, will require profound changes in the health care system and in how medical personnel are educated and trained. Over the last ten years, knowledge about many of the disease states common to the elderly and about the changes which occur with normal aging has expanded. Efforts will continue to understand fully the normal consequences of aging, why these changes occur, and what can be done to alleviate them.

The primary goal of the National Institute on Aging research programs is to extend the healthy middle years of life, thereby reducing the impact of the aging process. NIA-supported researchers are studying a broad range of topics relevant to this goal. Key among these topics is the continued effort to differentiate between normal aging and those disease states and conditions common to the elderly which are potentially preventable or reversible. The Institute supports a broad spectrum of research and training aimed at easing or eliminating the physical, psychological, and social problems which beset many older persons. Biomedical research efforts include studies on the diagnosis, etiology, and treatment of Alzheimer disease; the effect of immunodeficiency on health of the elderly; disorders such as incontinence; and exercise, cardiovascular health, and aging. The Institute also supports behavioral sciences research in such areas as cognitive and biopsychological aging and maintenance of independent and effective functioning of the elderly.

Disease prevention and health promotion, both especially relevant to the elderly, continue to be major Institute goals. Research on Alzheimer's disease is being pursued vigorously. The NIA is now into the second year of its large scale study on the health of aging black Americans. A program of research on the oldest old, that is, those over the age of 85, is being developed. The NIA recently reorganized its intramural research program to provide several new laboratories including the Laboratory of Molecular Genetics which will utilize the new recombinant DNA biotechnology. Extramural support for research using these new technologies is also expanding. Emphasis on manpower development programs in geriatrics and gerontology continues. Training of investigators in the field of aging research will continue to be one of the highest of Institute priorities.

Overall Budget Policy

The 1987 budget request for the National Institute on Aging of $145,829,000 is $2,438,000 below the FY 1986 revised estimate.

In FY 1987, the Institute will support a total of 490 research project grants for $84,248,000 compared with 480 research project grants for $86,092,000 contained in the revised FY 1986 estimate. This level will be achieved by limiting indirect cost and by negotiating direct costs downward. The request will support 145 competing project grants at an average cost of $162,090. This represents a 2.1 percent increase in direct costs over 1986 and a 10.4 percent reduction from full recommended levels. Historically, these reductions have averaged 3 to 4 percent. The request will support 345 noncompeting project grants at an average cost of $175,704. This represents a 4.4 percent decrease in direct costs from 1986 and an 8.6 percent reduction from full commitment levels. Historically, these reductions have averaged 1 percent.

The FY 1987 request will support all ongoing research centers, including the Alzheimer Disease Research Centers. In 1987, centers will be negotiated downward approximately 9.4 percent from the estimated full cost. This compares with a downward adjustment of 4.3 percent in FY 1986.

The Other Research category will be maintained at approximately the same levels as in the FY 1986 revised estimate. The total number of trainees supported in 1987 will be 195, 35 fewer than in 1986. The request will fund 42 contracts for $12,590,000 compared with 46 at $13,142,000 in 1986.

The 1987 budget request for Intramural Research is $20,250,000, an increase of $264,000 from the 1986 revised estimate of $19,986,000. The request for Research Management and Support is $8,172,000, an increase of $288,000 over the 1986 revised estimate of $19,986,000.

Program Accomplishments

Researchers now estimate that the annual direct cost for acute and long-term care of Alzheimer patients is $38 billion, with another $39 billion for "indirect costs" such as the cost of relatives visiting patients in nursing homes, transporting patients for needed medical services, and of premature death due to dementia.

The NIA supports major research activities on Alzheimer disease and related dementias in older people, including 10 Alzheimer Disease Research Centers. The five initial centers funded in FY 1984 have begun to produce important scientific knowledge. At one of the centers, it has been found that nuclear magnetic resonance (NMR) imaging can detect very early signs of small strokes or multi-infarct dementia and distinguish them from Alzheimer disease. This will enable physicians to institute appropriate treatments, thus preventing further deterioration. Research at another center is defining the genetic component of Alzheimer disease. At a third center, certain pathologic similarities between Alzheimer disease and Pick's disease, rare progressive dementia, have been identified.

Theories on the causes of Alzheimer disease have matured in a rich atmosphere of research on the neurosience of aging. Genetics, immunologic changes, atypical infectious agents, and environmental factors may all play a role. One group of NIA-supported researchers have preliminary evidence that Alzheimer disease may be a systemic metabolic disease, not simply a neurologic disorder. Several groups have identified and are now characterizing the abnormal proteins in the brains of Alzheimer patients. This may eventually lead to the development of a diagnostic test for this condition. An NIA grantee at the Bronx Veterans Administration Medical Center in New York has devised the Alzheimer Disease Assessment Scale which, though still in the trial stage, is hoped will provide valid and reliable measures of an Alzheimer patients' status.

More than 3 million persons over age 60 have systolic hypertension (i.e., systolic blood pressure of 160 mm Hg or above with a diastolic blood pressure below 90 mm Hg). These persons are at high risk for stroke, other cardiovascular diseases, and premature death. In FY 1984, the National Heart, Lung and Blood Institute and the NIA successfully completed a 5-year pilot project on isolated systolic hypertension in the elderly. The pilot study revealed that increased systolic blood pressure in older patients is responsive to antihypertensive medications. Experience demonstrated, however, that given the altered blood flow mechanisms in patients older then 60 years, gradual reductions in pressure are desirable. The pilot study also showed that the antihypertensive drug chlorthalidone (a diuretic) reduces systolic blood pressure in 88 percent of treated individuals. The adverse side effects of chlorthalidone are few and manageable, and patient compliance with both the medication and placebo regimens is high (85 percent). A major clinical trial building on the knowledge gained in the pilot study is now being conducted in 17 medical centers across the country.

Hip fractures are a leading cause of disability in older adults and account for a high percentage of nursing home admissions. Some estimates indicate that 10-20 percent of older persons suffering a broken hip will die within 6 months of the fracture. NIA researchers studying osteoporosis -- a disease resulting in brittle, fragile bones and therefore directly related to fractures -- have identified several subtypes including "post menopausal" osteoporosis associated with estrogen deficiency and a second type which may be caused by the body's decreasing ability to absorb calcium. Both types are potentially amenable to interventions which would slow the progress of the disease and reduce the risk of debilitating fractures.

In 1984, the NIA awarded the fourth of a series of NIA Established Populations for Elpidemiologic Studies of the Elderly (EPESE). This contract was for a large-scale study of the health of aging black Americans. The contract, one of the first of its kind, is currently in the field interview stage, with approximately 4,000 interviews anticipated. The analysis will provide descriptive material on health and health correlates among aging black Americans. In 1985, NIA began a special initiative on the Oldest Old. For the last several decades, the population over age 85 has been growing at almost three times the rate of that for all persons over age 65. Yet, at almost all levels, from the demographic to the physiologic, less is known about this age group than about any other.

Urinary incontinence is a common disorder that affects not only many institutionalized patients, but many community-dwelling men and women as well. Estimates indicate that about half of all nursing home residents and 7 to 14 percent of noninstitutionalized adults are incontinent of urine. Until recently, urinary incontinence has been generally neglected as an area of research. The NIA intramural research program supports an on-going project in this area and has recently established an inpatient geriatric continence project in cooperation with HCFA. The NIA and the Division of Nursing, Bureau of Health Professions, Health Resources Services Administration began supporting a series of clinical trials on urinary incontinence in the elderly in 1984. These trials hopefully will lead to effective treatments to eliminate or reduce the effects of this personally embarassing problem as well as aid in the reduction of nursing home care cost.

In 1985, the National Institute on Aging established an informal advisory group of leading molecular biologists to help identify the areas of greatest opportunity for research on molecular mechanisms of aging. The techniques of modern molecular biology are already providing powerful tools for exploration of gene structure and relationships between structure and function. Overall, the development of new biochemical techniques, such as recombinant DNA methods, is opening new opportunities for research. Classic theories of aging (e.g., free radicals, DNA errors and gene programming) are now susceptible to empirical tests.

National Institute on Aging

Aging

1987 Authorization: Indefinite.

Budget Authority:

1986 Appropriation	1986 Available after sequestering	1986 Revised Estimate	1987	Increase or decrease
$128,547,000	$123,076,000	$120,397,000	$117,407,000	-$2,990,000

Purpose and Method of Operation

The aging activity supports a multidisciplinary extramural research and training effort at universities, medical schools, hospitals and other institutions throughout the United States. Through this research the NIA seeks to develop a better understanding of biomedical, behavioral and social aging processes, to differentiate between the normal aging processes and disease states common to the elderly, and to achieve more understanding of the problems of older people. The long-range goal of these efforts, is to delay or avoid many of the debilitating effects of age, with consequent savings in both personal anguish and health expenditures. The aging activity consists of three programs: biomedical and clinical research; behavioral sciences research; and epidemiology, demography, and biometry.

Biomedical and Clinical Research Program

This program focuses on research related to the basic mechanisms of aging; normal changes in function with age; and clinical problems such as Alzheimer disease, urinary incontinence, and infections in older persons. It also has responsibility for the development, characterization, monitoring and distribution of animal, cellular, and biological materials necessary for the conduct of biomedical research. Funding mechanisms used consist of research and training grant awards, and research and development contracts.

Alzheimer Disease

By most estimates, some 2.5 million American adults suffer from Alzheimer disease. The cost of acute and long-term medical care for these patients is currently estimated at $38 billion, with another $39 billion in indirect costs. While no single medical test can diagnose Alzheimer disease, several successive generations of psychological tests have begun to focus more closely on the early and progressive signs of this condition. Other diagnostic tools are also becoming available. One NIA grantee is using nuclear magnetic resonance (NMR), the latest diagnostic tool, to examine patients with Alzheimer disease and other forms of dementia. This research indicates that the NMR has a unique ability to distinguish the brain's white and grey matter which allows it to pick up abnormalities that may indicate early multi-infarct dementia. Multi-infarct dementia is the second leading cause of dementia in older people. While NMR technology is still in its infancy, the finding of white matter lesions in otherwise healthy people suggests the potential of early diagnosis. If this is, indeed, an early indication of multi-infarct disease, diet and life style changes may prevent further damage.

In addition to neurofibrillary tangles and neuritic plaques, Alzheimer disease is characterized by deposits of amyloid fibers in the brain's blood supply. Another grantee has isolated and analyzed the amyloid proteins circulating in the bloodstream of Alzheimer patients and found a unique protein not seen in healthy individuals. Interestingly, the same protein appears in the amyloid deposits of Down syndrome, representing another link between Alzheimer and Down syndrome. This work suggests that Alzheimer disease is a systemic disorder, and may someday lead to a simple diagnostic test for the disease.

Research has also advanced on the causes of Alzheimer disease. Efforts are underway to discover the events that precipitate neurotransmitter changes and even cell death in Alzheimer disease. Research on enzyme activity, calcium transport, glucose metabolism and protein synthesis has led to studies of tissues, fluids, and cells outside the brain. Results from these studies have led to speculation that Alzheimer disease is a systemic metabolic disease, not simply a neurologic disorder. Other research has revealed a surprising similarity between Alzheimer disease and Pick disease, a rare progressive dementia. Recent findings show that abnormal proteins called paired helical filaments, previously thought to be unique to Alzheimer disease exist in the brain cells of Pick patients. This leads to the possibility that Pick disease may be a variant of Alzheimer disease and that the two may share a common cause. It has now been confirmed that when the central nervous system is exposed to aluminum over long periods of time, the result is neurofibrillary degeneration and ultimately cell death. An NIA grantee has found that aluminum binds to the protein calmodulin, thus impairing the protein's ability to regulate calcium levels in the cell. Calcium is similar in structure to aluminum and is vital to the life of the cell, but toxic in large quantities. The key to aluminum's deadly effect on nerve cells may thus be this breakdown of calcium metabolism at the cellular level.

Work continues on "slow virus" infections. It has now been shown that the protein (prion) involved in the animal disease "scrapie" is part of a larger protein present in both normal and infected cells. In normal cells, the larger protein is completely broken down by enzymes; in infected cells, defective breakdown leaves the prion intact. This protein has a fibrous structure that resembles certain filaments found in the brains of Alzheimer patients. Efforts are now focused on determining what happens to change a normal cell into an infected cell.

A discussion of possible causes of Alzheimer disease would not be complete without some reference to studies in the field of genetics. It now seems apparent that most Alzheimer victims do not simply inherit the disease from their parents. While there appears to be a familial form of Alzheimer disease in which the children of people with Alzheimer disease have a 50 percent chance of developing it later in life, it may be far more common for people to inherit a predisposition to the disease.

Osteoporosis

Osteoporosis is a degenerative bone disease which is directly related to fractures in elderly individuals. Two subtypes have been identified: "postmenopausal" osteoporosis is associated with estrogen deficiency, while the second type appears to result from a decreased ability to absorb calcium. Vitamin K deficiency may also be implicated in the disease. Vitamin K is essential for the synthesis of osteocalcin, a protein with calcium-binding properties needed for the mineralization of bone. Researchers have discovered that Gla (γ-carboxyglutamic acid), a component of osteocalcin, is excreted in the urine and may be a reliable indicator of vitamin K deficiency and the status of bone metabolism. The investigators hope to perfect a noninvasive method of detecting osteoporosis by measuring serum osteocalcin and urinary Gla.

The value of exercise for preventing bone loss in men has been demonstrated by NIA-supported researchers who found that strenuous exercises -- jogging and racquetball, for example -- performed at least once a week were related to higher bone mineral content. Another researcher is studying the effectiveness of estrogen combined with thiazide, a diuretic used for the treatment of hypertension. Women who have received this combination treatment and men who have taken thiazide on a long-term basis for hypertension show beneficial effects on bone mineralization. Studies are continuing on the potential therapeutic value of this drug.

Teaching Nursing Homes

The NIA now supports seven teaching nursing homes. Several important findings have come from these projects: Two Teaching Nursing Home projects are studying respiratory function in the elderly. Impaired respiration is involved in sleep apnea, a common condition among the elderly, in which breathing ceases for brief periods during sleep. This condition places subjects at increased risk of mortality. Researchers have found that sleep apnea in older persons is related to decreased respiratory muscle strength. Such age-related decreases can, however, be reversed by training programs. In addition, it has been shown that weight loss can reduce apnea in obese older patients. Another project has revealed that some older persons suffer drastic losses in strength in specific leg muscles and/or lose accurate sensation of leg position and that these persons are at markedly increased risk of falling. The identification of such specific factors may eventually lead to effective ways of preventing falls by reversing or compensating for these dysfunctions.

Molecular Genetics

NIA-supported research in molecular genetics continues to grow. Current priority areas include control of expression of genes related to aging, modification and rearrangements of DNA which accompany aging, and development of genetic theories of aging. The development of the powerful tools of molecular genetics, and their use to elucidate the structure of genes and the regulation of their expression hold great promise. It is reasonable to expect that "aging" genes or DNA fragments containing these genes can be identified and isolated using these techniques, as has been accomplished for the gene for Huntington's Disease. Such genes include both specific genes which affect longevity and genes which are defective in persons with various progeroid syndromes.

Behavioral Sciences Research

This program supports research on the psychological and social aspects of aging as a process; the behavior, attitudes, and status of older people; the relationships between aging individuals and society as a whole; and how these effect health and disease in older people. The principal funding mechanisms are research and training grant awards.

Behavioral Geriatrics

Behavioral geriatrics research is pointing to the significance of health promoting behaviors, social ties, and subjective psychological factors for morbidity and mortality among the elderly. Recent findings challenge previous notions about the futility of recommending changes in health behaviors in older populations. New longitudinal analyses from a large representative sample of adults reveal the continued association of traditional behavioral and social risk factors with morbidity, functioning, and mortality. This suggests that interventions to reduce these risk factors among the elderly may be efficacious in improving their health.

Interventions through training or through modification of environmental settings appear successful in reducing a variety of age-related decrements. For example, a workable drug management system can be designed that will prompt noncompliant patients to take prescribed medicines and dispense appropriate drugs at pre-programmed times. NIA-supported research is also demonstrating that behavioral strategies can reduce urinary incontinence in both community and nursing home residents, and that families can learn strategies to cope with behavioral problems of elderly relatives that might otherwise lead to premature institutionalization.

The Oldest Old

Descriptive data on the population over age 85 is beginning to accumulate, including evidence of the rapid growth rate of the very old population. The 85 and older age group, the most rapidly growing age group in the American population, increased by 141 percent between the 1960 and 1980 censuses. While the elderly population is itself aging, the oldest old population is sharing a similar fate. Between 1970-1982 the number of persons 95 and over increased at about twice the rate of the aggregate population 85 years and over. The centenarian population, while accounting for only 1% of the total over age 85 population, grew even more rapidly. Based on Medicare enrollment data the population aged 95-99 doubled between 1970 and 1982 but the centenarian population quadrupled, advancing from about 7,000 to 32,000.

Demographic analyses of the changing composition of the age 85 and over population find a number of trends in the sex ratio, the percentages of men and women who are married, in the sex and marital composition of the institutionalized population, and in living arrangements. For example, between 1930 and 1980 the sex ratio of males to females declined from 75.4 to 43.7. While 48% of all men 85+ were currently married in 1980 only about 8% of the women of this age group were married. During the period between 1970 and 1980 the percentage of women 85 years and over living in nursing homes and other long-term care facilities increased from 22% to 26%, while the percentage increase for males was from 14% to 16%. As is to be expected, the institutionalized population aged 85 years and over includes many more single (widowed, divorced and never married) males than the community population. Equal percentages of females in the community and in institutions are widowed, while substantially higher percentages of the institutionalized extreme-aged women had never married.

Minority Aging

Accurate knowledge of the elderly black has been hampered to some extent by poor data gathering techniques. A recent study has overcome some of these difficulties via new methods of identifying black households not only in high-density black areas but also in high-density white populations. The most common health problems reported by blacks are hypertension and arthritis followed by nervous disorders and circulatory problems. Other research indicated that for nearly one-third of Black elderly, social security and SSI payments are the sole means of support. Contrary to expectations, the more advantaged black elderly (those with higher income and education and younger age) receive more social supports than those whose needs are objectively greater.

Bereavement

Several longitudinal studies on spousal bereavement continue to highlight the ability of older people in general to adjust fairly rapidly to the loss of a spouse. They are also beginning to specify the conditions under which adjustment is more likely. One study has been following about 200 bereaved men and women over the first two years after their spouse's death. Less than a fifth of them experienced major difficulties associated with stress, coping, and depression. The survivor's sense of self-esteem proves to be best overall predictor of positive adjustment to bereavement. Moreover, when adjustment is difficult, it may reflect an undermining of the survivor's sense of social belonging and clarity of self-concept. Similarly, another longitudinal study is finding that survivors experience less depression when there have been specific preparations for bereavement, such as discussion of wills and finances, and where the survivor has a sense of closure in regard to his/her relationship to the deceased.

Epidemiology, Demography and Biometry Research Program

This program coordinates and conducts quantitative population-based research on health and disease in the aged, as well as demographic and economic analyses. The epidemiology program uses contracts and interagency agreements as funding mechanisms.

The NIA early recognized the lack of population estimates of prevalence and incidence of health problems and impairments of the elderly. It moved to meet this deficiency by initiating three population studies of the elderly (the Established Populations for Epidemiologic Studies of the Elderly, EPESE). These studies have now been established and are accumulating valuable prospective data. Analysis of this vast amount of data is expected to provide much needed information on the leading health problems of the elderly. These analyses will also identify associated factors for further investigation and generate hypotheses to define the actual risk factors of developing the health problems. The ultimate goals of this research are the transfer of knowledge to programs for prevention, and the provision of solutions for maintaining persons at their optimal ability for independent living and life satisfaction in the later years.

In 1985, a fourth EPESE project was initiated in Durham, North Carolina to study a predominantly black population of elderly persons. The first year, a planning year, included pretesting the baseline survey instruments and developing field procedures. The staff of this project has been integrated into the administrative scheme of the other three EPESE projects, a representative having been assigned to each of the major EPESE working committees.

Dementing diseases continued to be a major focus of activity during FY 1985. The study on the National History of Senile Dementia has produced rather startling results. Based on the approximately 500 subjects examined as part of the study, the prevalence of moderate to severe cognitive impairment in the noninstitutionalized East Boston population over 65 is about 10%, substantially higher than the 5% reported in other studies. In addition, approximately 80 percent of the persons identified as suffering from moderate or severe cognitive impairment were also identified as having Alzheimer disease (definite or probable on the basis of the clinical evaluation). Overall, these data suggest that rates of Alzheimer disease are substantially higher than expected among East Boston's elderly. Further analysis of these data are currently under way.

During this fiscal year the final data tapes from the NHANES I Epidemiologic Followup Survey became available and analyses began. Several committees with representation from all of the involved institutions met to discuss specific analyses, and several of these began. NIA staff are guiding or are involved in analyses related to mortality, hypertension, disability, weight, cognitive functioning, arthritis, hearing, sleep complaints, and other subjects. Plans have been initiated to publish a book which will summarize findings from the NHANES I Epidemiologic Followup Survey. This book will provide new information on the epidemiology of problems of aging and will inform the scientific community about the contents of the data set in order to facilitate its use by other investigators.

Training

In 1984, the NIA established new training awards in response to an earlier report prepared by an interagency task force on training in geriatrics and gerontology. Several of these awards were funded for the first time in FY 1985.

The Physician Scientist Award, both the individual award and the institutional award, was designed to train clinicians interested in aging in the skills required for independent research and to provide research experience in a fundamental science. In FY 1985, three individual Physician Scientist Awards and one institutional Physician Scientist Award were made.

The Complementary Research Training Grant Award follows the guidelines of the NRSA, Institutional Research Training Grant Award. It was designed to allow institutions with an ongoing training program funded by another Institute to submit an abbreviated application for adding a research training program in aging. One Complementary Training Grant was awarded.

agreements with investigators in the United Kingdom, Japan, and the United States to facilitate international research on aging.

Impact Data	1986 Appropriation	1986 Available after sequestering	1986 Revised estimate	1987
Res. Project Grants				
Number	504	504	480	490
Amount	$92,700,000	$88,771,000	$86,092,000	$84,248,000
Research Centers				
Number	12	12	12	12
Amount	10,396,000	9,949,000	9,949,000	9,812,000
Other Research				
Number	85	81	81	78
Amount	6,211,000	5,944,000	5,944,000	5,648,000
Training				
Number	240	230	230	195
Amount	5,507,000	5,270,000	5,270,000	5,109,000
R & D Contracts				
Number	48	46	46	42
Amount	13,733,000	13,142,000	13,142,000	12,590,000
Total	128,547,000	123,076,000	120,397,000	117,407,000

The Geriatric Leadership Academic Award invites academic health centers and other health professional schools to submit applications for the support of leadership activities in the development of research and research training in aging. This is an award, through an identified faculty catalyst, to develop an environment conducive and encouraging of faculty and student research. Two of these awards were funded in FY 1985.

During FY 1985, the NIA also developed procedures to fund approved but unfunded training slots on training grants paid by other Institutes (cofunding). The slots funded by NIA are filled by a trainee whose focus and program is on aging research. Fifteen trainees were supported on co-funded awards in FY 1985.

The variety and quantity of research possibilities in the field of aging continues to outstrip the number of trained investigators available. Consequently, the National Institute on Aging will continue to place great importance on its efforts to train and recruit top quality scientific investigators into the field of aging research.

Rational for Budget Request

The 1987 budget request for Aging of $118,069,000 represents a decrease of $5,730,000 from the 1986 level. The Institute will support 145 competing research projects in FY 1987, a decrease of 32 grants from the FY 1986 level of 177, plus an estimated 345 noncompeting awards. Twelve research centers including ten Alzheimer Disease Research Centers (ADRCs) will be supported in FY 1987. Support for training and research contracts will decrease by $133,000 and $1,063,000 respectively from FY 1986.

The NIA will attempt to maintain its research efforts in such key priority areas as Alzheimer disease, biotechnology, molecular genetics, and the oldest old. The five Alzheimer Disease Research Centers (ADRCs) funded in FY 1984 are already producing valuable insights into the early diagnosis and potential treatment of the disease. These five, plus the five ADRCs awarded in FY 1985, are expected to add significantly to the knowledge of Alzheimer disease over the next several years. NIA support of grants utilizing the new biotechnology has expanded over the last few years and is expected to continue to do so. Current priority areas in molecular genetics include control of expression in genes related to aging, modification and rearrangements of DNA which accompany aging, and the development of genetic theories of aging. Research on the oldest old will focus on studies of morbidity, mortality, and causes of death and also seek answers to such questions as what will the very old of the future be like — in health, functioning, values and attitudes?

During the upcoming fiscal year, the NIA will continue its current population studies (EPESE, NHANES I Followup, and the Framingham Dementia Study), and use these data sources to carry out a series of specific analyses. Partial data will also become available for analysis in FY 1986 from the Natural History of Senile Dementia Study, and from a neuropathologic/epidemiologic study aimed at identifying predictors of neurofibrillary tangle development (Honolulu Heart Autopsy Study). Activities aimed at providing future sources of information for analysis include the extension of the period of surveillance for EPESE subjects. Discussions are underway on the possibility of cooperative

National Institute on Aging

Intramural Research

1987 Authorization: Indefinite.

Budget Authority:

1986 Appropriation	1986 Available after sequestering	1986 Revised Estimate	1987	Increase or decrease
$20,915,000	$19,986,000	$19,986,000 (FTEs: 245)	$20,250,000 (245)	+$264,000 (—)

Purpose and Method of Operation

This activity supports the work of approximately 100 government scientists and distinguished visiting researchers, and their support staff. Approximately 75 projects are supported at the Baltimore Gerontology Research Center in an interdisciplinary environment, and in NIA's Laboratory of Neurosciences at the Clinical Center in Bethesda. The Baltimore Longitudinal Study of Aging, which currently has somewhat more than 1,000 participants, is a major part of this research effort.

The intramural program has two major components. The Gerontology Research Center (GRC) in Baltimore, along with its Bethesda-based Laboratory of Neurosciences, focuses on such specific research areas as clinical physiology, behavioral sciences, molecular aging, cellular and molecular biology, and comparative nutrition. The Gerontology Research Center has recently been reorganized to accommodate the nucleus of a Molecular Genetics Laboratory. This new laboratory will focus much of its efforts on application of new biotechnology methods to aging research. The second major component is the intramural portion of the epidemiology, demography, and biometry program. The staff of the epidemiology, demography, and biometry program supplement their own efforts with research and development contracts and interagency agreements which are funded from the aging budget activity.

Over the past year, the intramural Laboratory of Neurosciences has focused a major portion of its efforts on examining brain function during healthy aging and in disease states. The major thrust of the clinical program has been to measure cerebral metabolism by means of positron emission tomography (PET). In the last four years, the Laboratory of Neurosciences has established and validated the PET procedure so as to obtain accurate and consistent measures of regional cerebral metabolic rates for glucose (rCMRglc) under standardized and reproducible experimental conditions in humans. Scans of healthy individuals aged 21 to 83 years demonstrated that brain oxidative metabolism is age invariant in the resting state in healthy humans and is unrelated to neuropsychological performance. The age invariance indicates that, in the absence of disease, compensatory mechanisms exist in the senescent human brain to counteract effects of many of the morphological and neurochemical changes which have been reported to occur with age. PET scans of patients with Alzheimer disease (AD) of differing severity, as measured by scores on the Folstein Mini-Mental Test and Wechsler Adult Intelligence and Memory Scales, indicated that memory and cognitive deficits in mild-moderate AD patients are accompanied by reduced metabolism in association areas of the parietal lobes.

Seventeen patients with AD and 17 healthy controls were studied for rCMRglc, using a method of analysis which separates subjects into groups on the basis of similar patterns of metabolism, rather than diagnosis. Three groups were identified, two composed mainly of control subjects, and one of AD patients. The AD pattern consisted of an anterior to posterior gradient of decreasing metabolic activity, with relative sparing of anterior medial frontal, primary visual and subcortical regions. The pattern was not related to severity of dementia, and corresponded to independent findings of parietal lobe deficits in AD. Should this pattern prove unique to patients with AD, it may be of diagnostic significance.

Intramural scientists at the Gerontology Research center (GRC) have been investigating the therapeutic effectiveness of a combination of physical therapies and behavioral training procedures in elderly patients affected by either stress incontinence, bladder hyperreflexia, or urge incontinence. Of these three common types of urinary incontinence, stress incontinence is the most prevalent form, hampering almost half of all women at some time during their lives. It is characterized by the involuntary loss of usually small amount of urine. Patients with hyperreflexive bladders and urge incontinence often experience uncontrollable bladder contractions. GRC investigators worked with 39 elderly patients on an outpatient basis. Nineteen were identified as having stress incontinence; the remaining 20 had either bladder hyperreflexia or urge incontinence. Overall, about one-third of the patients achieved total continenece following therapy. Equally impressive, more than half experienced no accidents or only one accident per week after treatment. These encouraging results suggest that behavior therapy is an effective method for treating three major types of urinary incontinence in healthy, older men and women. Clinically, this cost-effective procedure has the potential for significantly reducing the medical and social problems linked to this frustrating condition.

An intramural Inpatient Geriatric Continence Project has now been established in cooperation with HCFA at the Francis Scott Key Medical Center in Baltimore. This project will explore the extent to which behavioral interventions can be used to reduce the prevalence of incontinence in nursing home residents. The behavioral techniques will include bowel or bladder/sphincter biofeedback, habit training and staff management procedures emphasizing strategies for enhancing patient independence.

The dietary variable has been re-introduced into the BLSA after a nine year hiatus in the men. No previous dietary information had been available on the women. Thus far 167 weekly diaries have been completed and returned. Software to access a database of over 5,000 food entries with more than 90 possible nutrient variables per food has been developed.

Recent findings from a fiber intake study of 499 men in the BLSA showed that cross-sectionally there was an increase in intake of 0.03 grams per year of age. Longitudinally, the increase was even greater; this increase occurred in all age groups. Thus, not only do older men consume more fiber, but there is also probably a secular or environmental effect as well. The question is: Is fiber intake related to health? To answer this fiber intake was correlated with certain coronary risk factors. There was a statistically significant favorable effect of diet on systolic and diastolic blood pressure and the fasting glucose level. In addition, there was a suggestively favorable effect on serum cholesterol and triglyceride levels and on glucose tolerance. In a related analysis, dietary variables were examined in a group of male BLSA subjects at age 53-95 years who subsequently died of cardiovascular disease; these were compared to matched disease-free survivors. Significant dietary differences were present in the men who died over age 75 as compared to their matched survivors: the group destined to die ate less fiber, fewer calories, and had a lower P/S fatty acid ratio. Thus, dietary risk factors have been shown to be present even into advanced old age.

Research by intramural investigators previously showed in a double-blind crossover study that digitalis could be discontinued for three months without adverse clinical effect and only minor changes in cardiac size and function in subjects with stable congestive heart failure (CHF) and sinus rhythm. Long-term follow-up of these patients has verified this favorable early response to digitalis withdrawal. A new study has now been initiated to investigate the effects of digitalis on aerobic performance and cardiac function during exercise, and its effects on cardiac rhythm in a new group of patients with chronic CHF and sinus rhythm.

Two new models are being prepared for incorporation into the larger NIA Macroeconomic-Demographic Model (MDM). A health expenditures model will be used to disaggregate expenses into various types — hospital care, physician's services, nursing home care, etc. The source of payment will be determined between direct out-of-pocket payments and third-party payments such as Medicare, Medicaid, and private health insurance. Health expenditures will be disaggregated by age group to reflect the variation by age among types of expenditures and the sources of payment. This research, utilizing new large data sets recently collected by the Federal Government and being made available to the public for the first time is of great potential importance to the nation's future health policies and the well-being of the elderly.

The second new model is a Consumer Expenditures Model of consumer demand behavior and the interrelationship between health and other consumer expenditures. This new consumption model will investigate the effects of prices, income, family size, age of household head, region of residence, race and type of residences on consumer expenditure shares. In addition to these new models, the overall Macroeconomic-Demographic Model will be updated and reviewed in order to take into account new data as well as new social security legislation.

Rational for the Budget Request

The 1987 budget request for Intramural Research is $20,250,000, an increase of $264,000 from the FY 1986 revised estimate of $19,986,000.

National Institute on Aging

Research Management and Support

1987 Authorization: Indefinite.

Budget Authority:

1986 Appropriation	1986 Available after sequestering	1986 Revised Estimate	1987	Increase or decrease
$8,352,000	$7,884,000	$7,884,000 (FTEs: 95)	$8,172,000 (95)	+$288,000 (—)

Purpose and Method of Operation

This activity provides the resources necessary to carry out the overall management and scientific direction of the Institute, as well as program guidance for the grants and contracts awarded under the aging activity. Functions include policy formulation; administrative services; financial and personnel management; program planning; coordination of the Institute's activities within the National Institutes of Health and with other federal agencies; disseminaton of research information; and scientific and business management of extramural grant and contract program. Salaries and related expenses are funded by this activity.

The first of a series of meetings of the Alzheimer Disease Research Center Directors was held in February 1985. Plans for developing a common clinical data gathering protocol were discussed. Work has begun to develop a coordinated data gathering procedure. The Evaluation Panel of the NIA Alzheimer Disease Program also held its first meeting in 1985. This panel is expected to produce a document identifying the strengths and weaknesses of the NIA extramural program on Alzheimer disease, and will serve as a guide for future program development.

A recent workshop on Altherosclerosis and Aging focused on the interaction of aging with the progression of atherosclerosis. It included epidemiologic, clinical, and experimental perspectives which will help identify worthwhile topics for further research. NIA staff are also serving on the planning committee for an National Heart, Lung and Blood Institute-sponsored workshop on coronary heart disease in the elderly. This workshop will focus primarily on clinical aspects of coronary heart disease including special problems of diagnosis and treatment in the elderly population. An NIA-supported workshop on the Molecular Biology of Aging has led to a program announcement on the "Molecular, Biological and Genetic Basis of Aging." It is anticipated that this announcement will be seen by molecular biologists with a wide variety of research interests, and that it will result in a significant number of research proposals which will be of interest to the NIA.

Two conferences are planned for FY 1986 on the diagnosis of Alzheimer disease. The first is a Conference on Heavy Metals of Trace Elements and Aging co-sponsored with the National Institute of Neurological and Communicative Disorders and Stroke, the National Institute of Mental Health, the American Association of Retired People, and the National Academy of Sciences. The second conference will focus on Diagnostic Criteria of Alzheimer disease and will be cosponsored by the NIA, the World Health Organization (WHO) and the European Network on Aging Research (EURAGE). Other workshops and conferences being considered for FY 1986 include such topics as the aging aorta, the aging immune system, calcium and aging, and the genetics of aging.

During FY 1986, the animal models contract program will expand through the hybrid rat contract and the biomarkers contract to provide alternatives to the Fisher 344 rat models. The addition of the new primate colony will provide a large mammal alternative model for development of NIA programs. The continued development of a strong mammalian genetics research effort will be a major program emphasis through concentration on recruitment of "modern" molecular geneticists to aging research, as well as continued emphasis on the development of genetic biomarkers of aging. Emphasis in the molecular biology program will be on the development of an active program involving recruitment and training of the pool of scientists needed to exploit the new opportunities of research in this area. Also to be pursued are Requests for Applications to stimulate research on diagnosis of Alzheimer disease and on the role of trace elements on aging processes.

During the past year, the NIA has made a strong effort to identify major areas for programmatic development and emphasis in research on the oldest old. Several avenues of research were found to be of particular importance. For example, it is critical to be able to predict with far more accuracy than in the past the numbers, demographic characteristics including the sex ratio, and active and dependent life expectancies of these individuals. While much of the immediately predictable growth in size of the elderly population is attributable to changes in the size of birth cohorts (the "baby boom" cohorts), decreased mortality at the older ages is playing a larger role in the growth of this unique population. Because of the singular growth in the size of the oldest old population, understanding the cross-national variability in patterns of morbidity and cause-specific mortality is increasingly important to the further understanding of people's lives at the older ages. An allied need is the improvement of the methodology of projection and forecasting techniques.

Efforts are currently underway for international collaborative work. Plans are being established with the United Kingdom which may allow for the collection of statistics comparable with the NIA Established Populations for Epidemiologic Studies of the Elderly. Ties have also been established with Japan which may lead to comparative studies related to dementia. There are possibilities of collaborative work with Sweden and Italy as well. Such projects could provide not only comparison of prevalence and incidence data but a test of replication of identified associated factors.

Rationale for Budget Request

During FY 1986, this activity will provide leadership and guidance for the Institute grant program. Efforts will continue toward development of more effective ways to address the programmatic and administrative needs of aging research.

The 1987 budget request for Research Management and Support is $8,172,000.

National Institute on Aging

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DETAIL OF PERMANENT POSITIONS

	1985 Actual	1986 Estimate	1987 Estimate
ES-4	4	4	4
ES-3	1	1	1
Subtotal	5	5	5
GS/GM-15	15	15	15
GS/GM-14	15	15	15
GS/GM-13	25	25	25
GS-12	25	25	25
GS-11	23	23	23
GS-10			
GS-9	24	24	24
GS-8	2	2	2
GS-7	28	28	28
GS-6	28	28	28
GS-5	25	25	25
GS-4	8	8	8
Subtotal	218	218	218
Grades established by Act of July 1, 1944 (42 U.S.C. 207):			
Assistant surgeon general grade	1	1	1
Director grade	8	8	8
Senior grade	7	7	7
Full grade	3	3	3
Subtotal	19	19	19
Ungraded	62	62	62
Total permanent positions	304	304	

TUESDAY, MARCH 18, 1986.

JOHN E. FOGARTY INTERNATIONAL CENTER FOR ADVANCED STUDY IN THE HEALTH SCIENCES

WITNESSES

DR. CRAIG K. WALLACE, DIRECTOR, JOHN E. FOGARTY INTERNATIONAL CENTER FOR ADVANCED STUDY IN THE HEALTH SCIENCES, NATIONAL INSTITUTES OF HEALTH, DEPARTMENT OF HEALTH AND HUMAN SERVICES

DR. JAMES B. WYNGAARDEN, DIRECTOR, NATIONAL INSTITUTES OF HEALTH

DR. MARK S. BEAUBIEN, DEPUTY DIRECTOR, JOHN E. FOGARTY INTERNATIONAL CENTER FOR ADVANCED STUDY IN THE HEALTH SCIENCES, NATIONAL INSTITUTES OF HEALTH, DEPARTMENT OF HEALTH AND HUMAN SERVICES

DR. CORALIE FARLEE, ASSISTANT DIRECTOR FOR PLANNING AND EVALUATION, JOHN E. FOGARTY INTERNATIONAL CENTER FOR ADVANCED STUDY IN THE HEALTH SCIENCES, NATIONAL INSTITUTES OF HEALTH, DEPARTMENT OF HEALTH AND HUMAN SERVICES

WILLIAM M. DOAK, EXECUTIVE OFFICER, JOHN E. FOGARTY INTERNATIONAL CENTER FOR ADVANCED STUDY IN THE HEALTH SCIENCES, NATIONAL INSTITUTES OF HEALTH, DEPARTMENT OF HEALTH AND HUMAN SERVICES

ROBERT C. MANGE, BUDGET OFFICER, JOHN E. FOGARTY INTERNATIONAL CENTER FOR ADVANCED STUDY IN THE HEALTH SCIENCES, NATIONAL INSTITUTES OF HEALTH, DEPARTMENT OF HEALTH AND HUMAN SERVICES

DENNIS P. WILLIAMS, ACTING DEPUTY ASSISTANT SECRETARY, BUDGET, DEPARTMENT OF HEALTH AND HUMAN SERVICES

Chairman NATCHER. We take up next the John E. Fogarty International Center. We have before the Committee at this time Dr. Craig K. Wallace, the Director of the John E. Fogarty International Center for Advanced Study in the Health Sciences.

Dr. Wallace, we are delighted to have you back before the Committee. Before you give us your statement, tell us who you have there at the table with you.

Dr. WALLACE. Thank you, Mr. Chairman.

On Dr. Wyngaarden's right is the Deputy Director, Dr. Mark Beaubien; on my left, Dr. Coralie Farlee, the Assistant Director for Planning and Evaluation; to her left, Mr. William Doak, the Executive Officer; and to his left, Mr. Robert Mange, the Budget Officer.

Chairman NATCHER. Thank you, Dr. Wallace.

Dr. Wallace, we will be glad to hear from you at this time.

Dr. WALLACE. Thank you very much, Mr. Chairman. I am very happy to be back here.

I would like to underscore certain statements that I made in our written statement. This time of budgetary restraints is certainly not a time to retreat from our international involvement, international perspective, and international leadership in the biomedical sciences.

We at the Fogarty International Center of the National Institutes of Health are a unique focus where we are able to establish and stimulate international collaboration at every level: scientist to scientist, institution to institution, and at Government to Government levels.

I also submit that when we think in terms of international research we do not compute that against domestic programs because all biomedical research in the larger sense has both a domestic component and an international component. There is much to be learned from study in both areas.

We conduct our activities through several program areas. Through our Advanced Studies Programs we address areas of concern that are not primary considerations of the other categorical institutes, such as preventable disabilities.

In this branch we are also coordinating the 1987 International AIDS Conference for the Public Health Service. This is another example of how we can bring the various resources of the NIH to bear on problems of international concern.

Through our Research and Awards Programs, which stimulate researchers going from the United States to work abroad and foreigners to come and work in the United States, we not only contribute to the development of these scientists and the laboratories, but such activity assures us of continued American leadership and influence in the biomedical research arena.

Also, it gives us an opportunity to study abroad on matters that we would not be able to adequately address here in the United States.

Finally, we are the operational link at the NIH for other domestic and international agencies. Currently, the NIH has linkages with some 70 countries. Exemplary of that is the Administration's priorities for China and India.

INTERNATIONAL CENTER

We, at the Fogarty, have been able to establish additional health scientist exchange programs through the Chinese Academy of Medical Sciences and Chinese Academy of Sciences in areas which supplement those under existing agreements of science and technology with China.

In India, we have assumed the technical management of the VAP or Vaccine Action Program. This brings together all the resources—fiscal and personnel—regarding vaccination in India, from basic research and development of new vaccines to delivery of vaccines and, indeed, study of the epidemiology of diseases.

Such activities are illustrative of the unique ways in which we hope to maintain NIH leadership. American leadership, in international biomedical research. For this, we are requesting $11,305,000.

I will be happy to answer any questions.

Chairman **Natcher**. Thank you, Dr. Wallace.

[The statement follows:]

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Statement of the Director
John E. Fogarty International Center
for Advanced Study in the Health Sciences

"We live in an era when the attention of the world is focused on the efforts of nations to find ways to work together in common purpose." These were the words with which Congressman John E. Fogarty opened his address to the World Health Assembly in 1962. They are no less appropriate today.

As Congressman Fogarty so aptly indicated, to attain the highest level of health worldwide, international medical research must be promoted in the interests of scientific advances. We must support medical research performed by foreign scientists whenever such studies will advance both the health status of the United States and the country in which the research is conducted. We must avail ourselves of the unequaled and often superior opportunities for our own research agendas. By uniting different approaches, greater progress can be made in a shorter amount of time--all mankind can benefit.

As we move into an era of constrained resources, we are giving careful attention to priorities and the effective use of those resources. We must assure that we do not retreat from our international perspective, involvement, and leadership. It is as important as ever, if not more so, that U.S. and foreign scientists continue to have opportunities to meet, discuss, and analyze their respective work, that U.S. and foreign scientists continue to have opportunities to collaborate in laboratories and share their unique talents toward common research objectives. U.S. and foreign scientists must continue to examine together those major health research issues that evolve and emerge as common, worldwide concerns.

As the focus for NIH international activities, the Fogarty International Center is unique in its responsibility to further international biomedical collaboration. It does this at every level--between scientists, between institutions, and between governments. Through its various programs that broaden international cooperation and agreement, the Fogarty International Center functions to maintain U.S. leadership in biomedical research while taking advantage of opportunities offered throughout the world that will enhance the health of the American people.

Under its Advanced Studies Programs, the Fogarty International Center is continuing its activities dealing with those infectious diseases considered candidates for foreseeable eradication. For example, there are in the world an estimated 1 million persons infected with yaws, a disease previously thought to be virtually conquered. In certain regions, particularly West and Central Africa, the situation is precarious; the proportion of children with infectious yaws is approaching that of pre-penicillin years. In 1985, as a followup to its 1984 international symposium on yaws and other endemic treponematoses, the Fogarty International Center initiated a meeting, in cooperation with the WHO and held in Indonesia, of Asian countries to stimulate and strengthen primary health care services by coupling curative treatment with prevention (immunization). Future activities include a 1986 meeting on yaws to determine the present epidemiological situation in the African region and to consider integrated control measures and the cost of implementing yaws treatment in children as part of the primary health care services in each country. The Fogarty International Center, together with a number of international organizations, is working to transfer state-of-the-art research results in the form of newly developed diagnostic techniques. We are also taking advantage of the research opportunities in this initiative to study penicillin resistance to the treponematoses--the agent causing yaws. Such research is important because of penicillin resistance in the closely related organisms that cause syphilis. It is further important to obtain this information to avert a potentially greater problem worldwide.

Another research effort in this program stems from the 1982 international symposium on poliomyelitis sponsored by the Fogarty International Center. Dr. Albert Sabin, senior expert consultant at the Fogarty International Center, is coordinating eradication activities for this infectious disease. He is also collaborating with colleagues to evaluate the aerosol vaccine and other approaches to measles vaccination, a direct outcome of the Fogarty International Center 1982 symposium on measles. These efforts with measles are particularly important to the United States: if susceptible non-immunized individuals either in this country or abroad are exposed to these viruses, the risk is great for individual infection or even outbreaks of an epidemic in a susceptible community.

The Fogarty International Center International Research and Awards Programs sponsor foreign scientists to work in U.S. laboratories and send U.S. researchers to foreign scientific institutions to conduct research of mutual interest, covering a wide range of scientific approaches. Their research is concentrated in areas of current global health concern--most generally neoplastic, metabolic, and infectious diseases. Such programs not only contribute to the development of scientists and their countries' resources but, more importantly, ensure the continuation of American influence and leadership in biomedical science.

In its role as the operational link between the NIH and other U.S. agencies and international organizations concerned with problems of world health, the Fogarty International Center facilitates the NIH's collaborative relationships in biomedical research with over 70 countries. Among these countries, China and India are of priority interest to the U.S. Government for maintaining strong cooperation in science and technology. With both countries, the NIH has major linkages of mutual benefit developed through the efforts of the Fogarty International Center. One of the several activities with China that we facilitated is the development of an understanding with the Chinese Academy of Medical Sciences to implement a health scientist exchange program that is intended to foster contacts between scientists in areas outside those under the existing agreements. We are also facilitating the implementation of collaborative activities under a separate agreement between the NIH and the Chinese Academy of Sciences, involving NCI, NIADDK, and counterpart institutions.

In the instance of India, the Fogarty International Center is coordinating NIH requirements for funding under the new U.S.-India Fund for Cultural, Educational, and Scientific Cooperation. This fund will support projects being proposed by NIAID, NHLBI, DRS, NIDR, and NLM and is replacing the former P.L.-480 Program for India. Thus U.S.-owned rupees will generate interest that can be used for U.S. projects. It is expected that about $1.2 million will be available annually for PHS health-related projects.

The Fogarty International Center plays a key role in the technical management of a new major program with India, the Vaccine

Action Program, which was announced by President Reagan and Prime Minister Gandhi following the Prime Minister's state visit in June 1985. This new program follows other successful collaborations in science and technology but differs in that it is focused on diseases that can be prevented through immunization programs rather than on a particular component of technology. It is comprehensive, covering a broad range of activities from basic research and development of new and improved vaccines to strengthening the quality control and vaccine manufacturing capability in the Indian private sector. The Vaccine Action Program incorporates interest both in science and technology collaboration and in immunization programs, the latter a critical feature of child survival programs throughout the world. In addition, the Vaccine Action Program will provide an opportunity for U.S. scientists who are working on vaccine development to pursue their studies through field study phase, an opportunity all too frequently unavailable.

In its role as the WHO Collaborating Center for Research and Training in Biomedicine, the Fogarty International Center sponsored --in cooperation with Gorgas Memorial Laboratory, the Pan American Health Organization, and others--a workshop on training needs in entomology for vector-borne disease research and control, held in Panama in October 1985. This project should be a significant factor in furthering regional and global strategies in manpower development for control of major vector-borne diseases. Further, in cooperation with the PAHO and the WHO, we are currently conducting a project in the Region of the Americas to identify patterns of international research collaboration between developed and developing countries as well as among developing countries. As a result of this project, we will be able to recommend strategies for strengthening health research capabilities of scientists to participate in the research mission of the NIH.

The Gorgas Memorial Institute and its Laboratory in Panama receive core support through the Fogarty International Center appropriation. The Fogarty International Center has supported site visits to the Laboratory to encourage the strengthening of their research and is urging the Institute to develop additional sources of funding so that the Laboratory may continue to be an important resource for the United States.

The various program activities of the Fogarty International Center are but threads of a tightly woven cloth encompassing much of the world by which NIH objectives are enhanced and shared. How else but with China and other countries will we learn about the variegated patterns and factors that influence the development of cancer? How else but with India and other countries will we be able to have a broad enough base to perfect new and better vaccines against infectious diseases? How else but with African and other countries can we trace the evolution of AIDS and its various manifestations? How else shall we be aware of research advances taking place in the Soviet Union and other Eastern European countries if it were not for our cooperative exchange agreements?

These activities were the reasons for the establishment of the Fogarty International Center in 1968 and its recent reconfirmation in legislation. These activities have been and will continue to be priorities of the Fogarty International Center. They are necessary and important to U.S. biomedical research interests and cannot be conducted without the Fogarty International Center.

In conclusion, I quote Congressman Fogarty: "Just as disease knows no boundaries, so also the benefits of medical research and indeed research itself can know no boundaries." To support the Fogarty International Center, we request $11,305,000 for FY 1987.

WALLACE, Dr. Craig K.
Director, Fogarty International Center, National Institutes of Health
Associate Director for International Research, National Institutes of Health

December 4, 1928. Woodbury, N.J. Married, two children.

Education. A.B. (cum laude), Princeton University, 1950. University of Virginia, School of Law, 1951. M.D., New York Medical College, 1955.

Professional History. 1955-1960, Intern, Medical Resident, and Chief Resident, Jefferson Medical College Hospital, Philadelphia, Pa. 1960-1963, Clinical Investigator, Naval Medical Research Unit (NAMRU) No. 2, Taipei, Taiwan. 1964-1969, Assistant Professor of Medicine, The Johns Hopkins University School of Medicine. 1964-1970, Assistant Professor of Pathobiology, The Johns Hopkins University School of Hygiene and Public Health. 1964-1966, Resident Coordinator and Head, Medical Program, The Johns Hopkins University Center for Medical Research and Training (CMRT), Calcutta, India. 1966-1969, Assistant Physician, The Johns Hopkins Hospital. 1967-1972, Associate Director, The Johns Hopkins University CMRT. 1969-1972, Associate Professor of Medicine, The Johns Hopkins University School of Medicine. 1969-1972, Physician, The Johns Hopkins Hospital. 1971-1972, Associate Professor of Pathobiology, The Johns Hopkins University School of Hygiene and Public Health. 1972-1974, Head, Research Detachment, NAMRU-3, Addis Ababa, Ethiopia. 1974-1976, Commanding Officer, NAMRU-5, Addis Ababa, Ethiopia. 1976-1978, Program Manager, Infectious Diseases Research, Naval Medical Research and Development Command, Bethesda, Md. 1978-1981, Chief of Internal Medicine, Naval Regional Medical Center, Camp Pendleton, Calif. 1981-1982, Director of Clinical Services, Naval Regional Medical Center, Jacksonville, Fla. 1982-1984, Commanding Officer, NAMRU-3, Cairo, Egypt.

Professional Associations. Fellow of the American College of Physicians; Fellow of Infectious Diseases Society of America; Fellow of the Royal Society of Medicine; Fellow of the Royal Society of Tropical Medicine and Hygiene; American Association for World Health; American Medical Association; American Society for Microbiology; American Society of Tropical Medicine and Hygiene; Association of Military Surgeons of the United States; The National Foundation for Infectious Diseases; National Council for International Health; The Professional Association of the Commissioned Corps of the U.S. Public Health Service.

Honors, Awards. Armed Forces Reserve Medal, 1975. Meritorious Service Medal, with Gold Star in lieu of the Second Award, 1976, 1984. Navy Commendation Medal, 1982.

GORGAS MEMORIAL INSTITUTE

Chairman **Natcher**. Dr. Wallace, if you will, bring us up to date on the activities of the Gorgas Memorial Institute. Are they making any progress in finding sources of support other than the approximately $2 million which we include in the bill each year?

What is the situation there, Dr. Wallace?

Dr. **Wallace**. Yes, Mr. Chairman, they are making progress. They have made several innovations during this last year.

In addition to the core support, of some $2 million, in fiscal year 1986 there is about $562,000 in competing NIH grants and another approximate $400,000 from other sources. Thus, about one-third of their operating budget comes from sources other than the core support.

There is now a paid president of the Gorgas Memorial Institute whose primary function will be fund-raising. At the Laboratory itself, they have reduced certain programs; they have not started certain initiatives, which I feel that they probably should; they also are not making any capital investments. They have a freeze on hiring.

There is much to be done, but they are making some progress.

Chairman **Natcher**. Does the research supported by the Gorgas Laboratory meet the same high standard as the other research supported by NIH?

Dr. **Wallace**. Well, as I said, Mr. Chairman, $562,000 is grants and contracts from the NIH. Indeed, it is comparable and competitive; actually, it is research that can only be done in Panama.

I might add, one very valuable resource at the Laboratory is a unique colony of Aotus monkeys where much of the drug testing for malaria drugs is performed by the United States Army. The Army, as well as the Navy, has a heavy investment in the Laboratory.

I submit it may be an old and rusty flagship, but is it the only flagship we have in Central America.

FOREIGN SCIENTISTS

Chairman **Natcher**. Your programs sponsor foreign scientists to work in United States laboratories and send U.S. researchers to foreign institutions to conduct research of mutual interest.

From which countries do most of the foreign scientists in these programs come, and further to which countries do most of the American scientists go?

Dr. **Wallace**. In the International Research Fellowship Progam, each of the 50 some countries with nominating committees may nominate up to six candidates per year. Over the almost 30 years of the program, most scientists have come to U.S. laboratories from Europe (especially Sweden, Finland, the United Kingdom, Italy and Spain) as well as from Japan, and Israel. The majority of the Americans in the Senior International Fellowship Program have gone to the United Kingdom and Switzerland.

INTERNATIONAL EXCHANGE

Chairman Natcher. Now, if you will, Dr. Wallace, give us one or two examples of how biomedical research has benefited from the international exchange of scientists.

Dr. Wallace. In the area of AIDS, Dr. Gallo has made the statement that without the input of the foreign nationals and investigators he would not have been able to make the progress that he has. Indeed, he refers to his laboratory as the "rainbow coalition." One of our senior Scholars-in-Residence is working very actively on the development of an animal vaccine for AIDS. In other countries, the epidemiology research that the National Institute of Allergy and Infectious Diseases has been able to do in Africa is giving us a basic pattern of the epidemiology of AIDS.

This is a very recent and ongoing example of such collaboration. Past experience with cholera abroad has been responsible for a whole new approach in the area of gastroenterology and, indeed, the development of the oral rehydration therapy.

There are many other examples, but these are two of the most telling.

Chairman Natcher. Dr. Wallace, we want to thank you and your associates for appearing before our Committee at this time in behalf of your budget request for the fiscal year 1987 for the John E. Fogarty International Center.

This, too, has been a good hearing, Doctor; and thank you very much.

Dr. Wallace. Thank you, Mr. Chairman.

[The following questions were submitted to be answered for the record:]

REAUTHORIZATION BILL

Mr. Conte. Doctor, did the recent NIH reauthorization bill, which, as you know, we had to override a veto on, did that bill change the scope or add any new direction to your operations at all? C-1

Dr. Wallace. The Health Research Extension Act of 1985, Section 482, recognized the Fogarty International Center in law for the first time. The functions authorized are quite similar to those established administratively for the Center in 1968.

GRAMM-RUDMAN-HOLLINGS REDUCTIONS

Mr. Conte. Where are you taking the Gramm-Rudman-Hollings reductions, and what will be the effect of these cuts in FY 1986? C-

Dr. Wallace. All of FIC's programs will feel the effect of the cuts mandated by Gramm-Rudman-Hollings, particularly the Scholars and fellowships programs. We will make fewer Senior International Fellowship awards and International Research Fellowship awards. Continuation awards for International Research Fellows will be reduced by approximately 7 and limited to a maximum of 4 months in duration. Other programs funded through the Research Management and Support category will be reduced. We will also particularly reduce the scope of the international assessment of research on rabies in our International Studies Program.

INTERNATIONAL RESEARCH AND AWARDS PROGRAM

Mr. Conte. Under the International Research and Awards Program, how much goes towards sponsoring U.S. scientists overseas, and how much to bring foreign scientists here? C-3

Dr. Wallace. In fiscal year 1985, the Fogarty International Center made 46 awards to U.S. scientists to conduct research abroad; the total dollars expended was $1.17 million. We made 100 awards to foreign scientists to come to the United States; the total dollars expended for these first year awards were $2.69 million.

RECIPROCAL FUNDING

Mr. Conte. Do any other countries operate programs that support U.S. scientists going abroad? C-4

Dr. Wallace. There are many countries that support U.S. scientists going abroad and not all of them are administered through the Fogarty International Center. Those countries for which we administer or facilitate programs for are Finland, France (2 programs), the Federal Republic of Germany, Ireland, Norway, Sweden and Switzerland. At least two other countries--Japan and Italy--support U.S. scientists to study in their respective countries.

FOREIGN SCIENTIFIC PROJECTS

Mr. Conte. Doctor, do you have any figures on how much of the regular NIH research budget supports foreign scientific projects? c-5

Dr. Wallace. Over the past five years, FY 1981 through FY 1985, the percentage of the total NIH appropriation devoted to international activities of all kinds has dropped steadily from 1.7 percent of the appropriation to 1.3 percent. About half of that--approximately $30 million in each year--has been expended to support foreign research grants, contracts, cooperative agreements or foreign components of awards made to U.S. investigators. The remainder of money spent on international activities supports research fellowships, scientific exchanges, travel and program management.

Mr. Conte. Which countries receive the most money? And, can you provide a list for the record showing the ranking of countries in order of dollars received? c-6

Dr. Wallace. In support of scientific projects (by either grants, contracts or cooperative agreements), over the last 5 years, scientists in the following five countries have received over one million dollars annually from funds appropriated to the NIH: Canada, Israel, the United Kingdom, Australia and Sweden.

Following is the rank order listing of countries and amounts whose scientists in FY 1985 received grant, contract or cooperative agreement support for research projects from monies appropriated to the NIH:

Canada	$7,453,000
Israel	3,490,000
United Kingdom	1,969,000
Australia	1,425,000
Sweden	1,067,000
China	827,000
Finland	651,000
Egypt	582,000
Denmark	494,000
Japan	429,000
Jamaica	396,000
Belgium	354,000
Italy	354,000
Argentina	301,000
Germany (FR)	296,000
Norway	217,000
Mexico	173,000
France	76,000
Switzerland	64,000
Netherlands	61,000
Yugoslavia	54,000
Ghana	45,000
Romania	38,000
Spain	32,000
Korea	19,000
Chile	8,000
Thailand	8,000

In addition to the above, the following amounts were awarded for research projects from Special Foreign Currency (P.L.-480) monies which are appropriated to the Office of International Health, PHS, and managed by the FIC for the NIH:

India	$4,246,000
Yugoslavia	314,000

HEALTH PROBLEMS OF FOREIGN COUNTRIES

Mr. Conte. Doctor, what are some of the major diseases coming from other countries that you see as potential threats to the U.S. population? C-7

Dr. Wallace. Among the diseases coming from other countries that pose a potential threat to the U.S. population are acute respiratory diseases, particularly influenza; sexually transmitted diseases including diseases caused by those strains of gonococci which are penicillin resistant; enteric pathogens resulting in diarrheal diseases; and tuberculosis which is being considered as the subject of a future Fogarty International Center effort.

Increases in international travel as well as immigration and emigration have resulted in an overall increase in the ability of microbes to cross national borders. The health status of the majority of people entering the U.S. each year is relatively unknown, particularly the health of undocumented aliens.

ACQUIRED IMMUNODEFICIENCY SYNDROME

Mr. Conte. I read in the justifications that you are sponsoring another world conference on AIDS. Where and when will this conference be held? C-8

Dr. Wallace. The conference will be held at the Washington Hilton Hotel from June 1-5, 1987.

Mr. Conte. We've read and heard a lot about the widespread problem of AIDS in Africa, particularly because the disease is spread heterosexually as well. Is AIDS as much of a concern in other countries as it is here in the United States? C-9

Dr. Wallace. To date, the Centers for Disease Control has announced that nearly 100 countries have reported patients having AIDS; the disease exists on every continent except Antarctica. In Western European countries there are fewer cases reported, possibly due in part to proportionately smaller national populations; however, health officials of the European countries are equally concerned about the spread of AIDS in their countries.

The lesser developed nations may ultimately experience a much more severe impact from AIDS than countries of the developed world. In this context, AIDS is now as much of a concern in these countries and health officials have already implemented preventive measures.

INTERNATIONAL CONFERENCES

Mr. Conte. How many international conferences does the Center support annually? Can you give us a list of those you will sponsor in 1986 for the record? C-10

Dr. Wallace. In FY 1986 the Fogarty International Center will sponsor approximately ten international conferences and workshops annually. Those which we have or will sponsor during FY 86 include: (1) Conference on Receptor Desensitization and Down Regulation: Biochemical Aspects and Clinical Implications; (2) Workshop on Strategies for Controlling Cancer through Genetics; (3) Conference on Yaws and Other Endemic Treponematoses; (4) Conference on Neuroaxonal Dystrophy and Axonal Transport; (5) Workshop on Antibiotic Use and Antibiotic Resistance Worldwide; (6) Workshop on Transactivators of Gene Transcription Involved in Transformation; (7) Conference on Biology of Carbohydrates; (8) Albert Sabin Symposium on Advances in Virology; (9) 6th International Conference on Cyclic Nucleotides and Protein Phosphorylation; (10) Symposium on Intermediate Filaments.

ADVANCED STUDIES PROGRAM

Mr. Conte. Under the Advanced Studies Program you support efforts focused on health issues of particular benefit to the United States. What are some of the special issues and activities targeted under the program in FY 1986? C-11

Dr. Wallace. Among the issues of particular benefit to the United States being targeted under the advanced studies program are AIDS, tuberculosis and rabies. The Fogarty International Center is playing a major role in the organization of the third International Conference on AIDS.

Each year approximately 30,000 Americans receive post-exposure rabies immunoprophylaxis in an attempt to prevent the fatal effects of being bitten by a rabid animal or an animal of unknown rabies vaccination status. Because of the excellent public health measures in the United States only 1-2 cases on average of human rabies fatalities are reported annually; nevertheless anti-rabies measures in this country costs approximately one hundred million dollars per year.

An FIC International Conference on Research towards Rabies Prevention is scheduled for November 1986.

GORGAS MEMORIAL LABORATORY

Mr. Conte. Doctor, can you update the table you gave to us last year on the sources of operating revenue for the Gorgas Laboratory in Panama? C-12

Dr. Wallace.

Gorgas Memorial Institute - Sources of Operating Revenue

	Actual FY 1985	Estimated FY 1986	Projected FY 1987
U.S. Government Core Support	$1,999,000	$1,913,000	$1,913,000
Research Grants and Contracts			
o World Health Organization	80,899	0	0
o Pan American Health Organization	7,875	0	0
o U.S. Army (drug evaluations)	259,714	244,084	38,376
o U.S. Navy (Training)	81,609	98,763	98,763
o National Institutes of Health	296,635	561,198	*429,319
o Other U.S. Sources	34,507	0	0
o Panama Sources	142,364	7,500	0
o Other	38,946	133,638	0
Other			
o Republic of Panama Contribution	10,000	10,000	10,000
o Other Panama Contribution		2,970	2,970
	$2,951,549	$2,971,153	$2,492,428

* Beginning 1/1/87 an additional 3-year sole source contract on HTLV-I with NCI of the NIH is expected to be awarded.

GORGAS MEMORIAL LABORATORY

Mr. Conte. We recently received a report from the Office of Technology Assessment talking about the great potential for technologies to control tropical diseases. What work does the Gorgas Laboratory conduct on tropical diseases, and what are your thoughts on the research potential in this area? C 12

Dr. Wallace. The research programs of the Gorgas Memorial Laboratory (GML) have traditionally been directed to improved control of the classical tropical diseases prevalent in Central and South America; e.g., arboviral diseases, including yellow fever, Venezuelan and St. Louis encephalitis; parasitic diseases such as malaria, Chagas' disease, and leishmaniasis; and diarrheal diseases of bacterial and viral etiology. Even today, the major emphasis of the Laboratory is on this group of diseases and a majority of its research projects relate directly to their control. Examples are: pre-clinical evaluation of new chemotherapeutic agents for malaria; clinical trials of drugs for cutaneous leishmaniasis; studies of the bionomics and vector competence of blackflies, the insect vectors of onchocerciasis; monitoring the population dynamics of the primate reservoirs and mosquito vectors of yellow fever; and identification and determination of the geographical distribution of Chagas' disease vectors. It is precisely on the results of studies of this kind that effective control programs are based.

In recent years the GML has begun to diversify its programs and to address other medical problems of the tropics, i.e., prevention and control of chronic diseases, acute respiratory infections, and sexually-transmitted diseases (including AIDS). These expanded activities reflect actions taken by Member Nations of the World Health Organization in support of the World Health Assembly resolutions to control the incidence of chronic diseases in tropical countries. Following are specific examples of how the potential of GML to address these diseases is currently being realized: leadership in a collaborative multinational research program on the epidemiology of cervical cancer in Latin America; collaboration with the Panamanian Ministry of Health in a screening program for the detection of sexually-transmitted diseases (including AIDS) in high-risk Panamanian populations; and initiation and participation of a long-term seroepidemiologic study in Panama of human T-cell lymphotropic virus type 1 (HTLV-I), the first human retrovirus shown to cause cancer.

Because of its geographic position in the isthmus, GML is also addressing major health problems in the tropics that transcend national boundaries. Steps have already been taken to strengthen the Laboratory as a regional site for research training and collaboration on prevention and control of health problems in the tropics. These actions are consistent with recommendations of the report by the Office of Technology Assessment.

INFORMATION DISSEMINATION

Mr. Stokes. How important is international cooperation in stimulating progress in the biomedical sciences?

Dr. Wallace. International cooperation is an integral part of the scientific mission of the National Institutes of Health and constitutes an important element in stimulating progress in the biomedical sciences. Such cooperation provides opportunities for (1) research in foreign countries having unique demographic, geographic, environmental, or socioeconomic features; (2) collaborative undertakings in which professional resources and costs are shared; and (3) exchange of up-to-the-minute research information at international conferences.

SCIENTIST EXCHANGE PROGRAMS

Mr. Stokes. With what countries does the Fogarty Center have cooperative research or scientific agreements? 5-1b

Dr. Wallace. The Fogarty International Center has responsibility for coordinating all collaborative research activities of NIH conducted under official bilateral agreements. In FY 1985, 56 agreements were in force between NIH and agencies or research institutions in 31 countries. Among the most active programs were those with China, France, India, Italy, Japan and the Soviet Union.

Mr. Stokes. What benefits can you cite from these international cooperative agreements? 5-1c

Dr. Wallace. Several significant research findings and benefits, resulting from collaboration under bilateral agreements coordinated by the Fogarty International Center, were described in the budget justification. Other examples are: (1) the observation, based on longitudinal studies supported by the National Institute of Child Health and Human Development in three developing countries (Guatemala, Bangladesh and India), that a mother's nutritional status before she conceives and the amount of weight she gains during pregnancy have an important impact on pregnancy outcome. When other factors such as maternal age, parity and socioeconomic status are held constant, it was shown that women who weigh more before conception and gain more weight during pregnancy are more likely to have a live birth; (2) the establishment of a relationship between dietary protein and the incidence of hypertension and stroke. Collaborative research between U.S. and Japanese scientists indicates that modification of dietary protein influences the calcium metabolism of heart muscle and, indirectly, the development of hypertension. This research has provided one of the few clues to the biochemical basis of hypertension; and (3) collaborative research supported by the National Cancer Institute, under agreements with China, France, Italy, Japan and the Soviet Union, on the clinical management, control and prevention of cancer.

VACCINE ACTION PROGRAM

Mr. Stokes. Please describe the role of the Fogarty Center in the Vaccine Action Program which has been initiated with India. 5-2a

Dr. Wallace. To date, the Fogarty International Center has hosted exploratory meetings between Indian and U.S. scientists and science administrators at which the Vaccine Action Program was shaped. A Fogarty International Center staff member has been instrumental in negotiating a Memorandum of Understanding with Indian institutions and with other U.S. Agencies which describes the various institutional roles in the program. Details of the administrative structure of the Program have not yet been concluded with Indian scientists and science administrators, but the program is certain to include the following elements for which the Fogarty International Center plays the leading role at the NIH. The program will emphasize research training for Indian scientists in the U.S., both at NIH laboratories and at U.S. universities. Conferences and workshops will be convened periodically to exchange technical information about progress in research of diseases which may be prevented with vaccines. Research activities will be coordinated with epidemiological and immunization activities to insure prompt utilization of research findings and to focus research on priority health problems. The Fogarty International Center is expected to represent the NIH in this network of PHS units which will form the U.S. core of the vaccine research and development components of the program.

Mr. Stokes. What do you hope to achieve through this collaborative effort? S-2b

Dr. Wallace. Through this collaborative effort, the Fogarty International Center hopes to secure significant additional opportunities for U.S. investigators to test their new and improved vaccines and diagnostic techniques in the field. Such opportunities, which are essential in vaccine research, are scarce for U.S. researchers. They can be efficiently promoted through collaboration with well trained foreign investigators who have ready access to field research opportunities and who wish to learn and share U.S. technological research expertise. We hope, also, to improve the efficiency with which this new collaboration with India is administered because of the support and approval which has been granted at high levels in the Indian government. Finally, through participation in a comprehensive program which coordinates basic and field research of vaccines with delivery of immunization services, significant improvements are expected in moving expeditiously from breakthroughs in basic research to application in the field and in targeting vaccine research and development more precisely on those health problems where research has the most to offer.

FIC FELLOWSHIPS

Mr. Stokes. How do you select the scientists who participate in the International Research Fellows Program and the U.S. Senior International Fellows Program? S-3a

Dr. Wallace. All candidates for these two programs must prepare applications that are subjected to the standard NIH peer review system. The initial scientific review is managed by the Manpower Review Section in the Division of Research Grants and the secondary review is managed by the newly established FIC Advisory Board. In addition, each applicant for the International Research Fellowship Program must be selected initially by an established scientific body in his or her country that we recognize as a

Nominating Committee. Likewise, an applicant for the Senior International Fellowship Program must first be nominated for the award by his or her academic dean. Thus, participants in these programs are rigorously selected for the award.

Mr. Stokes. How many such Fellows will be supported in these programs in FY 1986 and FY 1987? S-3b

Dr. Wallace. In fiscal year 1986, we plan to make 75 International Research Fellowship awards and 31 Senior International Fellowship awards. In fiscal year 1987, we plan to make 78 International Research Fellowship awards and 31 Senior International Fellowship awards.

BENEFITS OF FOREIGN RESEARCH AND EXCHANGES

Mr. Stokes. In what ways are foreign scientists contributing to U.S. goals in reducing morbidity and mortality from various diseases? S-3c

Dr. Wallace. Foreign scientists spend a short but very productive period of their research careers as International Research Fellows. While serving as fellows in U.S. institutions, they contribute to research on diseases that are of importance to U.S. citizens. Their findings are made known to the greater scientific community through publications in peer-reviewed journals and presentations at scientific meetings. Over seventy percent of International Research Fellowship recipients remain active as researchers upon return to their home country. In a report submitted to the Senate Appropriation Committee in February 1985, we listed the contributions of some former International Research Fellows. Most of these scientists have continued to conduct research in diseases that affect U.S. citizens such as diabetes, neurological disorders, cardiovascular diseases, nutrition, and viral infections. Their findings are published in professional journals--fellows who were in the program between 1966 and 1977 have over 27,000 citations in the NLM Medlars system.

Mr. Stokes. The FY 1986 appropriation of $1.999 million for the Gorgas Memorial Laboratory was reduced by $86 thousand under Gramm-Rudman. What impact will this reduction have on the operations of the laboratory? S-4a

Dr. Wallace. We believe that the 4.3% reduction ($86 thousand) of the FY 1986 GML appropriation ($1.999 million) will result in only minimal disruption to ongoing activities, although it will affect plans to conduct studies of immune responses to cutaneous leishmaniasis and malaria; and of insect vectors of river blindness (onchocerciasis).

Mr. Stokes. What major areas of research will be conducted by the laboratory this year? S-4b

Dr. Wallace. Major research being performed this year includes: arbovirus studies; ranging from research on modes of transmission and maintenance of St. Louis encephalitis virus to surveillance of yellow fever in Darien Province; cancer epidemiology, including collaborative multinational research on cervical cancer and seroepidemiological studies of the human T-cell lymphotropic virus type I; epidemiological and clinical studies of acute respiratory diseases in pediatric populations; and longitudinal studies of Chagas' disease.

ACQUIRED IMMUNODEFICIENCY SYNDROME

Mr. Stokes. To what extent is the Fogarty Center involved in research on AIDS? 5-5

Dr. Wallace. AIDS is the number one health research priority within the United States Public Health Service. The United States Centers for Disease Control coordinated the first major international conference on AIDS which was attended by approximately 3,000 health experts. The Pasteur Institute is coordinating a similar meeting in June 1986. With the worldwide research on AIDS moving at such a rapid rate, the FIC, at the request of the Director, NIH, has agreed to take the lead in coordinating the Third International Symposium on AIDS in collaboration with other NIH and PHS organizations. A Fogarty Scholar-in-Residence is conducting tests of a potential AIDS vaccine he developed utilizing the primate colony at the NCI's Frederick Cancer Research Facility.

FY 1987 BUDGET REQUEST

Mr. Early. Doctor, in your professional judgment, do you believe the FY 1987 budget request, which is a decrease of $186.8 thousand or 3.6 percent from the comparable FY 1986 post-sequestration level, and a decrease of $417 thousand or 8 percent from the comparable FY 1986 enacted level, will allow this country to maintain its leadership role in biomedical research? E-1

Dr. Wallace. The appropriation request for FY 1987 will have an impact on the country's ability to maintain its leadership role in biomedical research. The FIC supports several international research fellowship programs and conducts advanced studies in the health sciences. Reductions in these program areas will involve reductions of about 25 foreign scientists and 15 U.S. scientists as well as the postponement or reduction in the scope of studies in such areas as rabies, tuberculosis and an international conference on AIDS.

There are some indications that the leadership position in the United States in biotechnology is being challenged by such industrialized countries as Japan, Germany, and France. The 1983 report of the Office of Technology Assessment stated that even though the United States was currently the world leader in the basic sciences and the commercial development of new technology, continuation of this preeminence was not guaranteed. Given that other countries are increasing their resources devoted to biomedical research or have national policies to actively promote biotechnology, the U.S. leadership position is no longer assured.

FOREIGN SUPPORT OF BIOMEDICAL RESEARCH

Mr. Early. For the record last year you provided an estimate of the expenditures of several countries for biomedical research. Would you again this year provide us with your most recent estimate of expenditures for biomedical research for Japan, W. Germany, the Soviet Union, Switzerland, and Sweden. E-2

Dr. Wallace. As we indicated last year, it is very difficult to obtain information on expenditures of foreign countries for biomedical research. The data are not usually collected so that specific resources for biomedical research are able to be separated from the entire health budget (which also includes health care, clinical manpower development and may also include health services research). Biomedical research may also be reported as part of the larger science and technology expenditures which, therefore, also include engineering, physical, environmental, mathematical and social sciences. In some studies, only a portion of biomedical research expenditures are reported, e.g., the 1983 Office of Technology Assessment study on biotechnology. There is also the methodological issue of separating federal sources of support from other governmental and from private sources.

The study which the Fogarty International Center supported (in which the data were collected by the Organization for Economic Cooperation and Development and analyzed by Harvard University's Institute for Health Research) covered the biomedical research expenditures for the 10-year period from 1970 to 1980 for 19 industrialized countries.

The data we reported last year are, therefore, the most recent known to us. Those estimates of expenditures in 1980 (in U.S. dollars) for biomedical research and development are as follows:

		Rank
United States	$6,504,900,000	1
Japan	2,447,600,000	2
West Germany	1,578,900,000	3
The Soviet Union	7,000,000 (NSF estimate)	
Switzerland	297,500,000	8
Sweden	288,000,000	9

On a per capita basis, our study found that the first five countries in rank order of total (public and private) funding for biomedical research and development were: Switzerland, Sweden, the United States, West Germany, Netherlands, and France. Considering public funding alone on a per capita basis, Sweden ranks first, the United States second, West Germany fifth, Switzerland sixth, and Japan 10th. Slight differences in overall rankings from the results reported last year and here are due to final refinements in the data by the researchers between the preliminary and final project reports.

BUDGET IMPACT OF GRAMM-RUDMAN-HOLLINGS

Mr. Early. The amount being sequestered for the FIC in FY 1986 is $497,000, and the proposed budget increase for FY 1987 is $412,000. The net result being a decrease of $85,000 from the FY 1986 level. What program areas will be absorbing this net reduction? F 34

Dr. Wallace. All of FIC's programs will feel the effect of the net reduction, particularly the Scholars and fellowships programs.

Other programs funded through the Research Management and Support category will be reduced. These include the International Studies Program and the International Collaboration and Liaison Program.

Mr. Early. What impact will it have on your program? F 32

Dr. Wallace. We will make a total of 7 fewer Senior International Fellowship and International Research Fellowship awards. Continuation awards for International Research Fellows will also be reduced by 7 in number and limited to a maximum of 6 months in duration. We will reduce the scope of the international assessment of research on rabies in our International Studies Program. We will also limit the number of scientist exchanges with countries participating in the exchange program and reject any new initiatives proposed by the Department of State.

BHOPAL DISASTER

Mr. Early. Would you elaborate on what FIC's role has been in coordinating NIH's involvement in the activities related to the Bhopal disaster?

Dr. Wallace. In performing its function of facilitating international cooperation between NIH and the foreign biomedical research community, Fogarty International Center staff contributed to activities related to the Bhopal disaster in the following ways: scheduling visits of Indian scientists to NIH for discussions of follow-on studies; expediting travel by NIH scientists to Bhopal; distributing medical information on the Bhopal incident to appropriate NIH officials; and disseminating Department of State guidelines on involvement in Bhopal-related activities to NIH staff. Additionally, an FIC staff member serving as Science Attache at the U.S. Embassy in New Delhi, played a vital role in monitoring and reporting the events and in coordinating Public Health Service efforts in response to the disaster.

ACQUIRED IMMUNODEFICIENCY SYNDROME

Mr. Early. To what extent is the Gorgas Institute involved in studying the identification of the HTLV-III Virus in Panama? F-5a

Dr. Wallace. Since FY 1985 the Gorgas Memorial Laboratory (GML) has participated in a special AIDS Commission established by the Panamanian Ministry of Health to devise strategies to deal with the emergence of AIDS in Panama. In this context, GML provides: consultation on case detection and control activities; laboratory support, including confirmation of cases detected through the National Blood Bank screening program; clinical support; and contact tracing. GML has also conducted a survey for sexually-transmitted diseases, including HTLV-III infection in high-risk Panamanian populations. Epidemiological studies conducted in these populations have identified risk characteristics which suggest that HTLV-III infection will increase in Panama as it did in the U.S.

Mr. Early. What portion of the FY 1987 request will be directed toward this activity? F-5b

Dr. Wallace. The FY 1987 budget request for Gorgas is $1.913 million, of which $100,634 (5.4%) is being proposed to continue research on the HTLV-III virus.

INTERNATIONAL RESEARCH ACTIVITIES

Mr. Early. According to the justification 153 awards will be made in FY 1987 under the three International Research Activities programs. How many awards will be made under each program, and what is the average cost of these awards? F-6a

Dr. Wallace. We will make ten Scholar-in-Residence awards at an average cost of $55,800 per award. Approximately 78 new International Research Fellowships will be awarded at a cost of $27,600 each. An additional 34 continuation awards will average a prorated $28,400 in this program. Finally, we propose to make 31 Senior International Fellowships at an average cost of $28,400.

Mr. Early. How does this compare to the FY 1986 revised level and the FY 1985 level? F-6b

Dr. Wallace. Comparable levels for FY 1985 and FY 1986 are as follows: FY 1985: Scholars-in-Residence Program - ten awards at an average cost of $53,800; International Research Fellowships - 100 new awards at an average cost of $26,900; Senior International Fellowships - 46 awards at an average cost of $25,300. FY 1986: Scholars-in-Residence Program - nine awards at an average cost of $60,800; International Research Fellowships - 75 new awards at an average cost of $28,400; Senior International Fellowships - 31 awards at an average cost of $28,400.

FOREIGN BIOMEDICAL RESEARCH EXPENDITURES

Mr. Early. The justification states that the FIC is currently responsible for coordinating NIH's collaborative biomedical research activities under 56 bilateral agreements with 31 countries. In last year's record it stated NIH was participating in science and technology agreements with 27 countries. What are the four new countries which have begun working with the NIH? What is the nature of these new agreements? E-7

Dr. Wallace. The number 31 cited in the justification refers to countries with which NIH collaborates under all types of bilateral agreements (56), including umbrella science and technology agreements (government-to-government), health agreements (DHHS/Ministries of Health), and biomedical research agreements (NIH/counterpart institutions). The number 27 refers only to the government-to-government science and technology agreements (i.e., 27 of 56 total). No new science and technology agreements were signed during the past year nor did the number of countries with which NIH collaborates under official agreements increase over the previous year.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

John E. Fogarty International Center for Advanced
Study in the Health Sciences

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NATIONAL INSTITUTES OF HEALTH

John E. Fogarty International Center for Advanced Study in the Health Sciences

For carrying out the activities at the John E. Fogarty International Center, [$11,568,000] *$11,305,000* of which [$1,999,000] *$1,913,000* shall be available for payment to the Gorgas Memorial Institute for maintenance and operation of the Gorgas Memorial Laboratory. *(Department of Health and Human Services Appropriation Act, 1986.)*

NATIONAL INSTITUTES OF HEALTH

John E. Fogarty International Center for Advanced Study in the Health Sciences

Amounts Available for Obligation [1]

	1985 Actual	1986 Estimate	1987 Estimate
Appropriation....................	$11,728,000	$11,568,000	$11,305,000
Enacted administrative reduction......................	---	-17,000	---
Sequester order.................	---	-497,000	---
Subtotal, adjusted appropriation.......	11,728,000	11,054,000	11,305,000
Comparative transfers for changes in the central services financing mechnaisms and formulas:			
To:			
National Cancer Institute........	-8,000	---	---
National Institute of General Medical Sciences.................	-41,000	---	---
Subtotal, adjusted budget authority............	11,679,000	11,054,000	11,305,000
Unobligated balance lapsing....	-165,000	-161,000	---
Total, obligations	11,514,000	10,893,000	11,305,000

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[1] Excludes the following amounts for reimbursable activities carried out by this account: 1985 - $616,000; 1986 - $915,000; 1987 - $1,028,000

John E. Fogarty International Center for Advanced
Study in the Health Sciences

Budget Mechanism
(Dollars in thousands)

	1986 1/ Appropriation		1986 1/ 2/ Available after Sequestering		1986 Revised 1/ 2/		1987	
Research Grants:	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research Centers......	1	$1,999	1	$1,913	1	$1,913	1	$1,913
Other Research	155	4,622	148	4,423	148	4,423	153	4,557
					FTEs		FTEs	
Research Management and Support...........		4,930		4,557	58	4,557	58	4,835
Total............		11,551		10,893	58	10,893	58	11,305

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[1] Reflects an enacted administrative reduction of $17,000.

[2] Reflects a consultant services (Section 515 of the Treasury-Postal Service Appropriation Act, 1985) withholding of $161,000.

NATIONAL INSTITUTES OF HEALTH

John E. Fogarty International Center for Advanced Study in the Health Sciences

CROSSWALK - 1986 Appropriation

(Dollars in thousands)

	MECHANISM			
	Research Grants			
PROGRAM ACTIVITY	Research Centers	Other Research	Research Management and Support	Total
Gorgas Memorial Institute......................	$1,999	---	---	$1,999
International research activities......................	---	$4,622	---	4,622
Research management and support..	---	---	$4,930	4,930
Total......................	1,999	4,622	4,930	11,551

NATIONAL INSTITUTES OF HEALTH

John E. Fogarty International Center for Advanced Study in the Health Sciences

CROSSWALK - 1986 Available After Sequestering
and
1986 Revised Request

(Dollars in thousands)

	MECHANISM			
	Research Grants			
PROGRAM ACTIVITY	Research Centers	Other Research	Research Management and Support	Total
Gorgas Memorial Institute......................	$1,913	---	---	$1,913
International research activities.....................	---	$4,423	---	4,423
Research management and support..	---	---	$4,557	4,557
Total......................	1,913	4,423	4,557	10,893

NATIONAL INSTITUTES OF HEALTH

John E. Fogarty International Center for Advanced Study in the Health Sciences

CROSSWALK - 1987 Congressional Justification

(Dollars in thousands)

	MECHANISM			
	Research Grants			
PROGRAM ACTIVITY	Research Centers	Other Research	Research Management and Support	Total
Gorgas Memorial Institute	$1,913	---	---	$1,913
International research activities	---	$4,557	---	4,557
Research management and support	---	---	$4,835	4,835
Total	1,913	4,557	4,835	11,305

John E. Fogarty International Center for Advanced Study in the Health Sciences

Summary of Changes

1986 Current estimated obligations....................	10,893,000
1987 Estimated obligations...........................	11,305,000
Net Change..	+412,000

	1986 Base Amount	Change from Base Amount
Increases:		
A. Built-in:		
1. Within grade increase.........	2,273,000	+20,000
2. Federal Employees Compensation Fund increase.................	2,273,000	+ 2,000
3. FTS rate increase.............	244,000	+ 1,000
4. Payment for centrally furnished services..........	521,000	+19,000
5. Increased cost of supplies, materials and other expenses..	1,763,000	+75,000
Subtotal....................		+117,000
B. Program:		
1. Research centers:		
a. Noncompeting continuations...........	1,913,000	+1,913,000
2. Other research:		
a. Noncompeting continuations converting from competing status...................	886,000	+1,020,000
b Competing (new)..........	3,537,000	+3,537,000
3. Research management and and support:		
a. Program increase.........	4,557,000	+161,000
Subtotal..............		+6,631,000
Total, increases......		+6,748,000

Summary of Changes--continued

	1986 Base Amount	Change from Base Amount
Decreases:		
B. Program:		
1. Research Centers:		
a. Noncompeting continuations converting to committed...	1,913,000	-1,913000
2. Other research:		
a. Noncompeting completed or converting to competing status..................	886,000	-886,000
b. Competing completed or converting to noncompeting status..................	3,537,000	-3,537,000
Total, decreases........		-6,336,000
Total, net change.......		+412,000

John E. Fogarty International Center

Budget Authority by Activity
(Dollars in thousands)

	1986 Appropriation	1986 Available after Sequestering	1986 Revised		1987	
	Amount	Amount	FTEs	Amount	FTEs	Amount
Gorgas Memorial Institute............	$1,999	$1,913	--	$1,913	--	$1,913
International Research Activities...........	4,622	4,423	--	4,423	--	4,557
Research Management and Support..........	4,930	4,557	58	4,557	58	4,835
Total obligations........	11,551	10,893	58	10,893	58	11,305
Unobligated balance, lapsing..............		+161	--	+161	--	---
Total budget authority............	11,551	11,054	58	11,054	58	11,305

NOTE: All 1986 columns reflect an enacted administrative reduction of $17,000.

John E. Fogarty International Center for Advanced Study in the Health Sciences

Obligations by Object

	1985 Actual	1986 Estimate	1987 Estimate
Total number of full-time permanent positions.................	51	51	51
Total compensable workyears:			
Full-time equivalent employment.....	61	59	59
Full-time equivalent of overtime and holiday hours........	1	1	1
Average ES Salary.....................	$66,232	$62,920	$62,920
Average GS grade......................	9.14	9.14	9.14
Average GS salary.....................	$28,224	$26,813	$26,813
Average salary, grades established by act of July 1, 1944 (42 U.S.C. 207)...	35,361	33,593	33,593
Average salary of ungraded positions..	23,206	23,206	23,206
Personnel compensation:			
Permanent positions................	$1,525,000	$1,580,000	1,600,000
Positions other than permanent.....	281,000	300,000	310,000
Other personnel compensation.......	91,000	110,000	90,000
Subtotal, personnel compensation.	1,897,000	1,990,000	2,000,000
Personnel benefits.................	255,000	280,000	287,000
Benefits for former personnel......	4,000	3,000	3,000
Travel and transportation of persons..........................	69,000	100,000	100,000
Transportation of things...........	11,000	10,000	10,000

Rent, communications and utilities........................	229,000	244,000	248,000
Printing and reproduction..........	60,000	64,000	67,000
Other services:			
Centrally furnished services.....	505,000	521,000	530,000
Other...........................	1,288,000	1,223,000	1,466,000
Supplies and materials.............	63,000	64,000	64,000
Equipment.........................	43,000	58,000	60,000
Grants, subsidies & contributions..	7,090,000	6,336,000	6,470,000
Total................	11,514,000	10,893,000	11,305,000

NATIONAL INSTITUTES OF HEALTH
John E. Fogarty International Center for Advanced
Study in Health Sciences

Authorizing Legislation

	PHS Act/ Other Citation	U.S. Code Citation	1986 Amt. Authorized	1986 Estimate	1987 Amt. Authorized	1987 Budget Request
Research and Investigation...	Section 301	42§287b	Indefinite	$8,980,000	Indefinite	$9,392,000
International Cooperation.........	Section 307	42§287b	Indefinite		Indefinite	
"An act to authorize a permanent annual appropriation for the maintenance and operation of the Gorgas Memorial Laboratory"	PL. 70-350 as amended		$2,000,000	1,913,000	$2,000,000	1,913,000
Total Budget Authority				10,893,000		11,305,000

John E. Fogarty International Center for Advanced Study in the Health Sciences

Appropriations History

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation [1]
1978	8,489,000	8,483,000	8,483,000	8,483,000
1979	8,489,000	8,789,000	8,989,000	8,989,000
1980	9,095,000	8,989,000	8,989,000	8,987,000
1981	9,254,000	9,138,000	8,663,000	9,124,000
1982	8,438,000 [2]	9,589,000	9,589,000	9,205,000
1983	10,147,000	10,147,000	10,147,000	10,147,000
1984	9,189,000	11,584,000	11,088,000	11,336,000
1985	11,426,000	11,526,000	11,929,000	11,679,000
1985 Proposed Rescission	-241,000			
1986	11,464,000	11,529,000	11,606,000	11,551,000
1986 Sequester	-497,000			
1987	11,305,000			

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[1] Reflects enacted supplementals, and reappropriations.
[2] Reflects the September amendment; the original request was $9,589,000.

John E. Fogarty International Center for Advanced Study in the Health Sciences

(Dollars in thousands)

Justification

	1986 Appropriation	1986 Available After Sequestering	1986 Revised		1987	
			FTEs	Amount	FTEs	Amount
Gorgas Memorial Institute	$1,999,000	1,913,000	--	$1,913,000	--	1,913,000
International Research Activities	4,622,000	4,423,000	--	4,423,000	--	4,557,000
Research Management and Support	4,930,000	4,557,000	58	4,557,000	58	4,835,000
TOTAL	11,551,000	10,893,000	58	10,893,000	58	11,305,000

General Statement

Established in 1968, and created in law under P.L. 99-157 in 1985, the Fogarty International Center's mission is fivefold. The Fogarty International Center: (1) facilitates the assembly of scientists and leaders in the biomedical, behavioral, and related fields; (2) furthers international cooperation and collaboration in the life sciences through its research programs, conferences, and seminars; (3) provides postdoctoral fellowships for research experience in the United States and abroad and promotes senior scientist exchanges between the United States and other countries; (4) coordinates NIH activities and functions generally concerned with the health sciences at an international level; and (5) serves as a focal point for foreign visitors at the NIH.

The Fogarty International Center accomplishes its mission through four program activities. They are: (1) the Advanced Studies Programs, which support NIH research efforts by bringing scholars and other scientists to the NIH to study special issues and develop strategies for international health activities that benefit the United States; (2) the International Research and Awards programs, which facilitate the exchange of research experiences by either providing opportunities for U.S. scientists to work abroad, or for foreign scientists to pursue research interests in United States laboratories; (3) the International Coordination and Liaison Programs, which maintain liaison with inter- national components of the Department of Health and Human Services, Department of State, Office of Science and Technology Policy, U.S. Agency for International Development, and and other Federal agencies, foreign embassies, and multinational and foreign organizations; (4) the Foreign Scientists Assistance Programs, which provide coordination, visa assistance, and administrative services to visiting scientists and guest researchers.

Under the Advanced Studies Programs are the International Studies and the Scholars-in-Residence Programs. The International Studies Program addresses issues concerning international aspects of biomedical and behavioral research, research manpower training, and transfer of research results to bring new knowledge to bear where it will benefit international health. The program identifies barriers to the international transfer of research findings and develops methods to overcome these barriers.

The Scholars-in-Residence program invites a limited number of international scholars to come to the NIH for advanced study in a scientific environment that fosters the development of innovative approaches to research. Unencumbered by administrative responsibilities, the scholars have a unique opportunity to study subjects of their own choosing and to interact with the NIH scientific community. In an atmosphere that is conducive to cross-fertilization, ideas and information can be exchanged through collaborative research, lectures, and seminars.

The International Awards Program provides collaborative research opportunities for foreign scientists in the early stages of their careers. Not only do most of these former research fellows remain active as research scientists when they return to their home countries, but they also publish in journals of international importance, making their research findings readily accessible to U.S. scientists. After their fellowship year, a pattern of continuing relationship and collaboration with U.S. scientists emerges while former fellows become recognized experts in their areas of science, often as advisors to national and international science policy organizations and as participants on advisory boards of journals. Contacts among former fellows and national leaders who nominate them, in addition to U.S. hosts and other colleagues, help our country benefit from scientific advances being made elsewhere and cooperatively contribute to new knowledge of disease processes.

The U.S. Department of State has increased the number and scope of science and technology agreements with selected foreign governments. Through its International Coordination and Liaison Programs, the FIC is currently responsible for coordinating NIH's collaborative biomedical research activities under 56 bilateral agreements with 31 countries and for managing the Public Health Service's Health Scientist Exchange Program. Twenty-five of the formal agreements have been made at the government-to-government level for broad cooperation in science and technology. The international biomedical research activity that this collaboration makes possible benefits U.S. public health by expanding the base of knowledge required for solution of domestic health problems and by stimulating other countries to undertake research of potential value to our own public health pursuits. Many of the research projects ultimately being supported take advantage of unique opportunities in terms of unusual disease prevalence, population mobility, genetic determinants, and environmental risk factors.

An important foreign policy goal of the U.S. Government is to assist lesser developed countries to improve their health research and delivery capabilities. In its role as the World Health Organization (WHO) Collaborating Center for Research and Training in Biomedicine, the Center is working with WHO and the Pan American Health Organization to develop strategies for strengthening the research capabilities of countries in the Region of the Americas through international collaboration.

Within the context of institution-to-institution linkages among foreign and U.S. scientists, the FIC continues to provide the request for the Gorgas Memorial Laboratory core budget. This laboratory has had a 58-year history of institution-to-institution linkages both with the NIH and elsewhere in the United States and abroad. The achievements of the Laboratory have become well known to the international biomedical community.

The NIH has a 100-year history of international cooperation. By bringing scientists together to address particular problems, the FIC is able to stimulate new interest and bring renewed vigor to address various diseases that are potentially preventable in this decade, such as paralytic poliomyelitis, measles, yaws, and other treponematoses as well as preventable disabilities of concern to the United States and the world.

Overall Budget Policy

The 1987 budget request for the FIC is $11,305,000, an increase of $412,000 from the the 1986 current estimate.

The FIC will fund 153 senior and international research fellowships in 1987, 2 less than the 1986 current estimate. Stipends for the fellows will be the same as the 1986 level.

The Gorgas Memorial Laboratory will continue to be funded through the FIC budget. The 1987 level will be $1,913,000 which is the same as the amount provided in 1986.

A total of $4,835,000 will be available for research management and support, an increase of $278,000 over the 1986 level. This increase, in addition to helping defray mandatory and built-in increases, will support international coordination and liaison activities associated with Administration mandated bilateral exchanges between the United States and the Soviet Union.

Program Accomplishments

Each of the four major program areas of the Fogarty International Center is making significant contributions to the advancement of biomedical research and health by fostering international cooperation, as indicated in the following highlights.

Under its Advanced Studies Programs, the FIC has conducted several activities dealing with the eradication of infectious diseases. There are an estimated 1 million cases of yaws in the world today. In certain regions, particularly West and Central Africa, the situation is precarious, with the proportion of children with infectious yaws approaching that of pre-penicillin years. With a number of international organizations, the FIC is working to apply state-of-the-art research (e.g., the transfer of newly developed diagnostic techniques) to provide pragmatic strategies for eradication of yaws. In 1985, as a follow-up to its 1984 international symposium on yaws and other endemic treponematoses, the FIC initiated a meeting, in cooperation with WHO and held in Indonesia, of Asian countries to stimulate and strengthen primary health care services by coupling curative treatment with prevention (immunization). Future activities include a 1986 meeting on yaws to determine the present epidemiological situation in the African region and to consider integrated control measures and the cost of implementing yaws treatment in children as part of the primary health care services in each country.

Another follow-up effort stems from the FIC-sponsored 1982 international symposium on poliomyelitis. Dr. Albert Sabin, FIC senior expert consultant, is coordinating eradication activities for this infectious disease, particularly in the developing world. He is also collaborating with colleagues to evaluate the aerosol vaccine and other approaches to measles vaccination, a direct outcome of the FIC 1982 symposium on measles.

A Fogarty Scholar-in-Residence from Scotland, a leading international authority on viruses and vaccines, has collaborated with scientists in the National Cancer Institute by coordinating an international group of researchers developing a vaccine for AIDS. Preliminary results show that an immuno-stimulating complex, a pseudo virus, containing the large envelope glycoprotein of HTLV-III has produced a good antibody response in primates using two different strains of HTLV-III. The immunized primates will be challenged with virus-infected cells to see if they have protective immunity. If successful, an improved vaccine prepared from recombinant synthesized envelope coat protein will be tested.

The FIC's International Research and Awards Programs, which bring foreign scientists to U.S. laboratories and send U.S. researchers to foreign scientific institutions to conduct research of mutual interest, cover a wide range of scientific approaches. Most of these are concentrated in areas of current health concern such as cancer, diabetes, and infectious diseases. For instance, in 1985, a Senior International Fellow, working with researchers at the National Institute of Cholera and Enteric Diseases in India, examined the source and spread of a unique clone of antibiotic-resistant Shigella dysenteriae. On the basis of this work, the researchers concluded that ampicillin-resistant strains were preferably selected in the 1984 diarrheal epidemic of West Bengal by the frequent use of ampicillin.

In its role as the operational link between the NIH and other U.S. agencies and international organizations concerned with problems of world health, the FIC facilitates the NIH's collaborative relationships in biomedical research with over 70 countries. A number of significant research advances were made under bilateral agreements coordinated by the FIC. Among these countries, China and India are of priority interest to the United States Government for maintaining strong cooperation in science and technology. With both, NIH made major contributions of mutual benefit through the coordinating role of the Fogarty Center as noted below.

In addition to a number of activities under the formal U.S.-P.R.C. agreements, the FIC was able to effect a modification of overall policy such that important NIH cooperative projects could be undertaken with China outside of those prescribed by formal agreements. These have included NCI clinical trials and projects of NIADDK.

Other notable advancer are:

- The FIC is facilitating the development and clearance of an agreement between NEI and the Zhongshan Ophthalmic Center in Guangzhou.
- An understanding has been reached with the Chinese Academy of Medical Sciences to implement a health scientist exchange program that is intended to foster contacts between scientists in areas outside those under the existing agreements.
- The FIC is facilitating the implementation of collaborative activities under a separate agreement between the NIH and the Chinese Academy of Sciences, involving NCI, NIADDK, and counterpart institutions.

The FIC has also contributed to collaborative research efforts with India. Following the announcement during the Reagan-Gandhi Summit in June that the Indo-US S&T Initiative (STI) would be extended for 3 years, the FIC worked with NICHD, NEI, and NIAID to ensure that the NIH projects would continue and to resolve any budgetary difficulties related to the extension. In addition, the FIC represented the NIH at the Indo-US S&T Subcommission Meeting in New Delhi last April. The Subcommission was pleased to note that cooperation in health had nearly doubled since its previous meeting and that many of the STI projects were an outgrowth of work under the Subcommission's auspices.

The Fogarty International Center plays a key role in the technical management of a new major program with India, the Vaccine Action Program, which was announced by President Reagan and Prime Minister Gandhi following the Prime Minister's state visit in June 1985. This new program follows other successful collaborations in science and technology, but differs in that it is more broadly focused on diseases which can be prevented through immunization programs rather than on a particular component of technology. It is comprehensive, covering a broad range of activities from basic research and development of new and improved vaccines to strengthening the quality control and vaccine manufacturing capability in the Indian private sector. The Vaccine Action Program incorporates interest in both collaboration in science and technology and in immunization programs - a critical feature of child survival programs throughout the world.

The two principal U.S. agencies in the Vaccine Action Program are the Public Health Service and the Agency for International Development. A Fogarty health scientist will be one of two Department officers who will administer the program, while the Director of the Fogarty International Center will represent the NIH on the Joint Working Group which will oversee the program.

The Vaccine Action Program will provide an opportunity for U.S. scientists, who are working on vaccine development, to pursue their studies through the field study phase, an opportunity which is frequently unavailable to them. Working jointly with the Agency for International Development offers each agency access to expertise not readily available in one or the other alone. Thus, the Vaccine Action Program will provide the technical expertise of the Public Health Service, while university scientists, supported by NIH programs, and the Agency for International Development will provide access to bilateral collaborative opportunities with Indian scientists.

The FIC is also coordinating NIH requirements for funding under the new US-India Fund for Cultural, Educational, and Scientific Cooperation. The Fund will cover projects being proposed by NIAID, NHLBI, DRS, NIDR, and NLM. The Fund is replacing the former PL-480 Program for India. U.S.-owned rupees will generate interest which can be used for U.S. projects. In FY 1986, and in subsequent years, it is expected that about $1.2 million will be available for PHS health-related projects.

The FIC has coordinated and facilitated NIH involvement in activities related to the Bhopal disaster, which remains a highly sensitive issue between our two countries. Through the FIC's staff representative (and Embassy science attache), meetings between NIH officials and the Indian Council for Medical Research were arranged to discuss mutual research interests, to coordinate the visit of Indian scientists involved in methyl isocyanate studies, and to plan for a visit to India by NIAID, NHLBI, and NIEHS officials.

Under FIC's WHO Collaborating Center for Research and Training in Biomedicine, the FIC sponsored, in cooperation with the Gorgas Memorial Laboratory, the Pan American Health Organization, and others, a workshop on training needs in entomology for vector-borne disease research and control, held in Panama in October 1985.

John E.Fogarty International Center for Advanced Study in the Health Sciences

Gorgas Memorial Institute

1987 Authorization: Indefinite.

Budget Authority:

1986 Appropriation	1986 Available after sequestering	1986 Revised Estimate	1987	Increase or decrease
$1,999,000	$1,913,000	$1,913,000	$1,913,000	0

Purpose and Method of Operation

The Gorgas Memorial Laboratory continues to be an important resource located in a tropical environment for the conduct of research on diseases prevalent in the Latin American region and of importance to the interests of the National Institutes of Health, other U.S. and international agencies, and countries of the region. In addition to its programs of research, it will be continuing other services of disease surveillance, consultation and referral, training, and library resources.

Rationale for the Budget Request

The Laboratory has four major divisions -- Epidemiology, Laboratory Sciences, Environmental Biosciences, and Clinical Investigation--that are further subdivided into departments.

The Division of Epidemiology will continue its work on cervical cancer in Latin America. Under a $1.1 million 3-year research contract from the National Cancer Institute, studies are being conducted in collaboration with institutions in Panama, Costa Rica, Colombia, Mexico and the United States. Studies will also continue on human T-cell leukemia viruses, including the identification in Panama of HTLV-III, the causative agent of AIDS, and cases of AIDS.

The Division of Laboratory Sciences, which maintains surveillance of yellow fever in the region, will intensify its efforts because of the cyclical nature of the disease and occurrence of cases in adjacent areas.

Because cutaneous leishmaniasis and Chagas' disease are major parasitic diseases in large areas of Latin America, they remain principal subjects of laboratory, clinical and epidemiologic study by several departments of the Laboratory. Therapeutic drug trials will continue in cooperation with the Santo Tomas Hospital, Panama.

During 1985, the Fogarty International Center assisted the program planning efforts of the Laboratory through the sponsorship of two scientific panel site-visits, one in parasitology and the other in virology and epidemiology. These provided advice on future research directions and technologies. A scientific site-visit on clinical research is being planned for 1986.

For 1987, the request for the Gorgas Memorial Institute is $1,913,000, which is the same as the amount provided in 1986.

Impact Data	1986 Appropriation	1986 Available after sequestering	1986 Revised estimate	1987
Res. centers				
Number	1	1	1	1
Amount	$1,999,000	$1,913,000	$1,913,000	$1,913,000

John E. Fogarty International Center for Advanced Study in the Health Sciences

International Research Activities

1987 Authorization: Indefinite.

Budget Authority:

1986 Appropriation	1986 Available after sequestering	1986 Revised Estimate	1987	Increase or decrease
$4,622,000	$4,423,000	$4,423,000	$4,557,000	+134,000

Purpose and Method of Operations

The FIC supports basic and clinical research activities in the life sciences through a series of intramural and extramural fellowships. These programs are designed to: (1) bring world-renowned scholars to the NIH to stimulate discussion and collaboration in rapidly advancing fields of research; (2) enable established U.S. investigators who wish to expand their capabilities and knowledge to work in foreign laboratories; and (3) provide opportunities to young foreign scientists to work with established investigators in the United States on topics of mutual interest.

Rationale for the Budget Request

The 1987 budget request for International Research Activities is $4,557,000, an increase of $134,000 from the 1986 level. This increase will be used to fund approximately five additional fellowship awards, for a total of 153 fellowship and scholarship awards.

Scholars-in-Residence

The Fogarty Scholars-in-Residence represent an unsurpassed intellectual resource for the NIH intramural community. These scholars, each of whom is an outstanding contributor in a particular area of biomedical research, are an integral part of the Center's Advanced Studies Program. They bring to the NIH community new concepts and research hypotheses that in turn stimulate other ideas. Through regularly scheduled formal and informal seminars during their stay, they are able to interact and influence a far greater number of senior scientists than would be possible through any other type of program. Many scholars, in fact, apportion some of their time among two or three laboratories in as many institutes, and spend the rest of their time writing, organizing conferences, or developing new theories in their field of research. Their ability to become directly involved in several areas of NIH research activity is one of the most beneficial aspects of the program.

The collected bibliography continues to grow; 45 papers have been published by scholars since the last report was written. An Indian scholar published a series of papers on development of vaccines against leprosy in collaboration with collaborators in the United States and India. A Japanese scholar wrote a book summarizing knowledge about information-bearing peptides, their characterization, and synthesis. These peptides include many hormones and neurotransmitters. He also published on the development of synthetic antigens for preparation of hepatitis vaccines.

A U.S. scholar devoted his last two terms to studying the relationship between cellular oncogene expression and hematopoetic development in collaboration with a member of the NHLBI staff. He also organized a series of guest lectures in the Stone House on hemoglobin assembly, related to a conference held at the FIC in 1984. The rest of his time was devoted to preparation of a book, Hemoglobin, Molecular, Genetic and Clinical Aspects, using the collections available in the National Library of Medicine as reference material. This scholar's research at NIH is directly related to the thalassemias and other diseases caused by abnormal hemoglobins that are widespread in many parts of the world.

Other scholars studied a variety of topics including the regulation of gene expression during embryogenesis; development of more sensitive methods for determining the structure of complex polysaccharides; chemotactic substances and the migration of metastasizing cancer cells; role of receptor molecules in growth of tumor cells; characterization of defensive chemicals in insects; analysis of proteins related to ossification of developing bone tissue; development of special adsorbents for purification of complex subcellular organelles; and the role of disturbances of axonal transport processes in nerve cells related to specific neuroaxonal dystrophies.

Beyond their research and writing, the scholars continue to give numerous seminars in many NIH laboratories and were able to reach different groups of intramural scientists. They also will continue to give public lectures under the co-sponsorship of the appropriate institutes and the Foundation for Advanced Education in the Sciences.

International Research Fellowships

The International Research Fellowship Program was established to attract to the United States foreign biomedical researchers in the developmental stage of their postdoctoral careers for an interim of collaborative research with an American biomedical scientist at a domestic academic institution. Researchers from diverse academic and intellectual traditions and at creative stages in their careers have the potential of bringing novel approaches to refractory problems and thus can make significant contributions to problems deemed of current importance by the U.S. biomedical science community. It is a condition of the awards that the foreign scientists must return to their home countries and to positions in which they can utilize the training and experience obtained during the tenure of their fellowships.

There are both reciprocal short- and long-term effects of this program. During the tenure of their fellowship, most fellows are able to advance their research to a point that results can be published in refereed U.S. and internationally recognized journals, rather than foreign-language national journals of limited circulation. The research findings of this program become immediately available and a part of the U.S. scientific information base.

The research experience, knowledge, and concepts acquired by fellows during their fellowships lead to improved research environments in their home institutions upon return and and thus help to develop new centers of biomedical research significance. The professional associations of individual scientists fostered through this program evolve into expanded associations and solid linkages with the biomedical science community of many countries. Many former fellows whose research careers were stimulated by this program attain positions of influence in academic and research institutions, such as deans of medical schools, directors of research institutes, advisors to international organizations, and members of scientific societies and editorial boards of journals, including those in the United States.

The research of international fellows spans the scope of the biomedical sciences from clinical or patient-oriented studies to fundamental physical-chemical studies at the molecular and nuclear levels. The challenges of cancer, diabetes, and immunological aspects of these and other diseases are the focus of the preponderance of fellows.

For example, interferons have been used in both the prophylaxis and treatment of a number of human viral infections. There are three sub-types of interferon, IFN-α, IFN-β, and IFN-λ. Because it is found in individuals suffering from viral infections, interferon is believed to be an active part of the immune system. The sub-type IFN-λ is the only one that can be heat-induced. An International Research Fellow from Mexico, working with scientists from Indiana University, pursued a research program that attempted to understand the molecular mechanism of

IFN-λ induction and action. Using the techniques of genetic engineering technology, these researchers were able to demonstrate: (1) in a herpes virus-transferred lymphoblastoid cell line, the increased antiviral activity registered upon heat-induction was due to de novo synthesis of an IFN-λ-like lymphokine, and (2) the heat-induced IFN may be a different type of IFN-λ since it, the physico-chemical and biological properties are somewhat different than known isolates. In addition to these observations, preliminary work was begun on purifying and characterizing the heat-induced protein.

Senior International Fellowships

The Senior International Fellowship Program is designed to provide an opportunity for U.S. biomedical and health science researchers established in their careers to devote a period of time to advanced study or to participate in a collaborative research activity with an associate in a foreign institution. The program is intended to promote the exchange of ideas and information about current problems and advances in biomedical sciences or the conduct of a significant research study, through sustained personal contact with imminent peers, the objective being to contribute to the fellows' potential for enhancing research, teaching, and clinical programs upon return to their home institutions. Fellows are selected on the basis of the recognition afforded them by their peers, their home nominating institutions, and invitations from foreign host institutions.

The scientific and clinical accomplishments and professional stature of fellows in this program are such that the participants are welcome in foreign laboratories that are at the forefront of the investigation of disease and normal life processes, diagnosis, treatment, and prevention measures. The intellectual stimulation of study in such an academic environment with foreign colleagues accelerates the introduction of the most recent tentative and confirmed information and concepts into the research, teaching, and clinical care programs in the fellows' home institutions and into the U.S. biomedical and health science community.

This program gives highly sought-after senior U.S. biomedical researchers and clinical investigators--burdened with academic responsibilities, leadership roles in professional societies, and government consultant activities--a brief respite during which they can devote their attention and efforts to strictly intellectual pursuits, such as: synthesizing current knowledge about disease processes and examination of the validity of current concepts about these; conceiving new hypotheses about biological processes and developing new methods of testing them; anticipating potential offerings of science; and projecting the ethical, philosophical, sociological, economic, and humanitarian aspects of such possible developments before they are suddenly thrust upon society through some unexpected technological advance.

Through the association of senior scientists during the tenure of a fellow, aspiring young scientists in the host laboratory are identified and reciprocal exchanges of young staff between the U.S. and foreign laboratories are frequently arranged. The career development of such young researchers is also a by-product of the Senior International Fellowship Program, which serves to further solidify the bonds with the bioscience community of the foreign country.

The neurosciences and investigations of the brain represent one of the most intriguing and potentially most important frontiers of contemporary biomedical science. This field is well represented in this program. The immunological process whereby Lymphocytic Choriomeningitis virus, a common infective viral agent in mice, causes central nervous system disease is being studied in Denmark. Schizophrenia and related mental disorders are being studied in England through use of genetics and family twins, imaging of the brain, and relationships between the brain and behavior in order to elucidate the pathophysiology or causes of mental illness. A fundamental study of electron transfer in a biologically active agent called quinone, which occurs naturally in foods or is produced by burning organic substances, is contributing to the field of bioenergetics and understanding of the effect of exercise on biochemical changes with age. These are only a few of the many examples of collaborative studies which might be cited.

Impact Data	1986 Appropriation	1986 Available after sequestering	1986 Revised estimate	1987
Scholars-in-Residence	$ 573,000	$ 548,000	$ 548,000	$ 573,000
Senior Int'l Fellowships	1,014,000	970,000	970,000	1,014,000
Int'l Research Fellowships	3,035,000	2,905,000	2,905,000	2,970,000
Total	4,622,000	4,423,000	4,423,000	4,557,000
Res. project grants				
Number	155	148	148	153
Amount	4,622,000	4,423,000	4,423,000	4,557,000

John E. Fogarty International Center for Advanced Study in the Health Sciences

Research Management and Support

1987 Authorization: Indefinite.

Budget Authority:

1986 Appropriation	1986 Available after sequestering	1986 Revised Estimate	1987	Increase or decrease
$4,930,000	$4,557,000	$4,557,000	$4,835,000	+278,000
		(FTEs: 58)	(58)	(0)

Purpose and Method of Operation

The budget request for research management and support provides positions and funds for the International Coordination and Liaison Programs, International Studies Program, and the Foreign Scientists Assistance Programs. These funds also support salary and support costs for overall management and direction of the Center.

Rationale for the Budget Request

The budget request for research management and support for 1987 is $4,835,000 and provides an increase of $278,000 over the 1986 funding level.

International Coordination and Liaison

The International Coordination and Liaison Programs provide staff support for the role of the FIC Director as the Associate Director for International Research, NIH. These programs facilitate the implementation of U.S. Government obligations resulting from formal treaties and bilateral agreements with foreign governments and assists the categorical institutes in expanding their research base through cooperative agreements with foreign institutions. To carry out these activities, program staff maintain liaison with DHHS international components, the Department of State, and the U.S. Agency for International Development and other Federal agencies, foreign embassies, and multinational and foreign organizations. Staff advise the Director, NIH, and the Directors of NIH Bureaus, Institutes, and Divisions on research opportunities, and on the development of international policies, procedures, and activities relating to biomedical research.

International Studies

The International Issues Study Program addresses research topics of critical importance to the health of the people of the world. International conferences, organized and directed by the FIC, have focused world-wide attention on a number of diseases that could be candidates for eradication if certain research problems were solved, appropriate resources allocated, and appropriate control strategies adopted. Eradication of a disease can only be considered in an international context. Without worldwide cooperation, even the most vigorous attempts at disease eradication by a majority of the countries of the world must ultimately fail if the disease can find areas in which it can flourish.

The FIC and the World Health Organization are jointly coordinating studies for potential integrated infectious disease control efforts and an African-wide regional meeting on yaws and other endemic treponematoses. The FIC, NIH, and the World Health Organization are the principal organizers of this meeting in which to date 19 Member States of the African Region have agreed to send representatives; it is anticipated that representatives of 40 nations will be in attendance. This is a follow-up to an earlier FIC conference on this subject which also included a similar regional conference held in July 1985 in Cipanas, Indonesia.

In 1987 the FIC will organize and sponsor, in collaboration with NIAID and others, a world meeting on AIDS. This is a continuation of earlier international conferences on this subject which began in April 1985, coordinated by the Centers for Disease Control.

Foreign Scientists Assistance

The FIC provides direct support to the NIH Intramural Research Program through its administration of the NIH Visiting Program and the foreign scientists portion of the NIH Guest Researcher program. The Visiting Program enables intramural laboratories to bring foreign scientists to NIH to assist staff in carrying out their research programs. Foreign Guest Researchers are given the opportunity to use the facilities and resources at the NIH which are not available to them in the home country. These programs serve two goals: first, to provide a source of talented scientists to facilitate the research of the laboratory; and second, to provide a base for future scientific collaboration.

Impact Data	1986 Appropriation	1986 Available after sequestering	1986 Revised estimate	1987
Research management and support				
Amount	$4,930,000	$4,557,000	$4,557,000 (FTEs:58)	$4,835,000 (58)

John E. Fogarty International Center for Advanced Study in the Health Sciences

Detail of Permanent Positions

	1985 Actual	1986 Estimate	1987 Estimate
GS/GM-15	7	7	7
GS/GM-14	3	4	5
GS/GM-13	3	4	3
GS-12	4	4	5
GS-11	0	1	0
GS-9	7	7	7
GS-8	2	0	0
GS-7	3	4	5
GS-6	9	11	10
GS-5	6	3	3
GS-4	2	1	1
GS-3	0	0	0
Subtotal	46	46	46
Grades established by the Act of July 1, 1944 (42 U.S.C. 207):			
Director Grade	4	4	4
Full Grade	1	1	1
Subtotal	5	5	5
Total permanent positions	51	51	51

TUESDAY, MARCH 18, 1986.

NATIONAL LIBRARY OF MEDICINE

WITNESSES

DR. DONALD A.B. LINDBERG, DIRECTOR, NATIONAL LIBRARY OF MEDICINE

DR. JAMES B. WYNGAARDEN, DIRECTOR, NATIONAL INSTITUTES OF HEALTH

KENT A. SMITH, DEPUTY DIRECTOR, NATIONAL LIBRARY OF MEDICINE

DR. HAROLD M. SCHOOLMAN, DEPUTY DIRECTOR FOR RESEARCH AND EDUCATION, NATIONAL LIBRARY OF MEDICINE

KENNETH G. CARNEY, EXECUTIVE OFFICER, NATIONAL LIBRARY OF MEDICINE

MARK J. ROTARIU, BUDGET OFFICER, NATIONAL LIBRARY OF MEDICINE

DENNIS P. WILLIAMS, ACTING DEPUTY ASSISTANT SECRETARY, BUDGET, DEPARTMENT OF HEALTH AND HUMAN SERVICES

OPENING REMARKS

Chairman NATCHER. Now we take up the budget request for the National Library of Medicine. We have before the Committee Dr. Lindberg.

Dr. Lindberg, it is a pleasure to have you before our Committee again. Before you give us your statement, if you will please tell us who you have there at the table.

Dr. LINDBERG. Yes, sir. To Dr. Wyngaarden's right is Dr. Harold Schoolman, Deputy Director for Research and Education; on my left is Mr. Kent Smith, Deputy Director; to his left is Mr. Mark Rotariu, our Budget Officer; and to his left is Mr. Ken Carney, our Executive Officer.

Chairman NATCHER. We are delighted to have all of you before the Committee. We will be glad to hear from you at this time.

Dr. LINDBERG. Thank you so much.

Mr. Chairman, it is a special pleasure for me to appear before you on this the NLM's 150th anniversary. We are honored that you and your colleagues have enacted a joint resolution designating 1986 as the sesquicentennial year of the National Library of Medicine.

President Reagan, in issuing a proclamation about the Library, said, "American citizens, for whom the health of their loved ones is always a primary concern, can take great pride in their National Library."

Mr. Chairman, for 150 years, the Library has quietly gone about the business of providing medical information to America's health professionals. Today, it stands as the world's preeminent medical library, a tribute to the foresight of past generations of health professionals and of legislators.

From a handful of books in the Surgeon General's office to a collection of 3½ million housed in two modern buildings on the campus of the National Institutes of Health, the National Library of Medicine is a institution in which all Americans can take pride.

The last two decades especially have been a period of unparalleled expansion in the Library's responsibilities. A series of challenges in health communications has been met with a series of prudent and successful responses.

In 1965, deteriorating medical libraries and their inability to meet the needs of the biomedical community led the Congress to enact the Medical Library Assistance Act. This law not only improved the state of medical libraries, but made possible the creation of a regional medical library network for disseminating biomedical information that has served the Nation well for 20 years.

Subsequently, concern with the quality of the environment led a presidential commission to recommend a special Federal Toxicology Information Program. This was established at the National Library of Medicine in 1967.

The potential of new computer and communications technologies subsequently led the Congress to call for a major research and development program at the Library: namely, the Lister Hill National Center for Biomedical Communications. Since 1968, this organization has played a key role in improving information services for medical research, education and health care delivery.

The Library's pioneering computerized information system, MEDLARS, went on line in 1971. It now provides 3 million searches each year to American health professionals. Later this year we will add our six millionth record to the data base.

There can be no doubt that the information needs of the health care professions will change dramatically in the years ahead. These changes will spring from new information generated by our national investment in research and also from the opportunities afforded us by evolving computer and communications technologies.

The National Library of Medicine is, today, engaged in a series of activities that will allow the Library to shape, rather than be shaped by, these changes.

First, a formal 20-year plan is being developed for the Library with the assistance of panels of experts from around the Nation. These experts are ranging widely in considering how the Library should address the future from the role of traditional collections and services to computerized banks of actual scientific data as opposed to bibliographical citations to medical informatics research and how it can influence medical education and health care.

I can give you some preliminary findings, if you wish, but in any event I look forward to bringing you the final version at the hearings next year.

Second, the Library, with the encouragement of the Congress, has embarked on an ambitious project to develop a Unified Medical Language System. The lack of a practical common terminology greatly impedes the efficient retrieval of biomedical information.

The system now under development will permit a health care professional or scientist to move smoothly from one data source or file to another in order to gather information pertinent to a particular problem of a patient. The Library's effort to develop such a system is a joint one with the American Medical Association, university research groups, scientific professional societies and Federal experts.

Essential to creating any such integrated system is a way for the individual physician or scientist to dial directly to NLM services. A new microcomputer interface—that is, a computer diskette—that will do exactly that has been developed and is not being made available through the National Technical Information Service. A health professional will now be able to easily dial up on the telephone and get the information he or she wants directly.

The implementation of a Unified Medical Language System would help to accelerate progress in other developments of national importance. These include the Integrated Academic Information Management Systems—IAIMS—and programs to improve the state of medical informatics.

The IAIMS concept is to use computer and communications technologies to create systems in academic centers that integrate a variety of information in support of health research, education, patient care and management. The IAIMS grants are designed to produce exemplary advanced prototype systems at a small number of outstanding medical centers. Several such centers have been funded and it is hoped that they will serve as models for others.

Medical informatics, another beneficiary of the Unified Medical Language System, is a multidisciplinary research field involving the integration of computer and information sciences, medicine, engineering and management science. This work provides the growing scientific and theoretical basis for the application of computers and automated information systems in medicine.

One product of such research will be a computerized system with which human users can consult interactively much in the same way that physicians and scientists consult with their colleagues.

A second important research area has been emphasized to us by our long-range planning panels. They note that the ambitious goals lately announced to understand the origins of cancers through molecular biology and to map the entire human genum are dependent upon major advances in information systems technology. These future information systems to support discovery in molecular biology and biogenetics are as essential as the much-to-be-desired breakthroughs at the laboratory bench and in the clinic.

In addition, the preservation initiative should be reemphasized. The National Library of Medicine's primary function is its statutory responsibility to acquire and preserve library materials pertinent to medicine.

Although the Library devotes significant efforts to the carrying out of its preservation responsibilities, the majority of library materials in existence today are printed on high-acid-content paper that is destined to disintegrate. NLM faces the inevitable loss of much of its collection unless preventive action is taken immediately.

Data gathered by an NLM preservation planning team showed that 8.8 percent or 113,000 volumes in the collection are so brittle that they must be copied to another medium to ensure long-term preservation of the information they contain. The remaining volumes must be deacidified to prevent rapid deterioration.

This is a problem faced by all large research libraries and we are optimistic that the Library of Congress may allow NLM to use its planned mass deacidification facility when that facility becomes operational in the next few years.

Additional funds provided by Congress in FY 1986 will allow NLM to award a major contract for the microfilming of deteriorating materials; and there is other progress being made in the preservation initiative.

Library Operations is the component responsible for NLM's basic mission to build, maintain and provide access to the world's largest collection of biomedical literature. In 1985, the Library added some 293,000 items to the collection and, for the first time, acquired a limited number of computer software packages for use by patrons.

MEDLARS, NLM's computerized data base, not only provides on-line searching services, but produces many bibliographical publications such as the *Index Medicus* and various specialized literature-search reports. In addition to providing access to the literature through publications and on-line data bases, NLM helps health professionals to obtain copies of documents in the collection.

The Lister Hill National Center for Biomedical Communications is an intramural research and development component of the Library. The Center is performing research in a number of promising areas.

One of these is the use of optical disks for electronic document preservation. I will give a little bit more detail in the written remarks, Mr. Chairman.

Other areas of research at Lister Hill include knowledge representation; computer-based systems to examine methodologies for electronic organizing machine readable data bases to increase the productivity of NLM's indexing and cataloging; and development of prototype computer-assisted instructional materials for education.

The Toxicology Information Program, to mention an additional operation, has two primary objectives: to create computerized toxicological data bases, and to provide toxicological information products and services to the scientific community. These services are made available through a variety of on-line information retrieval files, through query response and interagency collaborative projects.

Work continues on development of the microcomputer work station that is used for retrieving information needed to respond to emergencies involving hazardous chemicals.

In summary, the mission of the National Library of Medicine—the rapid and efficient dissemination of biomedical information—is an integral part of the research process. Without dissemination, the fruits of research have little value.

The Library's innovative programs, some of which I have described for you today, exploit the latest advances in technology and information science and thus assist the Nation's biomedical research and health care apparatus to operate more effectively and efficiently.

Mr. Chairman, the request for the National Library of Medicine for fiscal year 1987 is $56,408,000, an increase of $1,086,000 from the fiscal year 1986 adjusted appropriation level. I shall be pleased to answer further questions.

Chairman NATCHER. Thank you, Dr. Lindberg.

[The statement follows:]

DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH

Statement of the Director
National Library of Medicine

Mr. Chairman and distinguished members. It is a special pleasure for me to appear before you during this, the NLM's 150th anniversary. We are honored that you and your colleagues have enacted a Joint Resolution designating 1986 as the Sesquicentennial Year of the National Library of Medicine. President Reagan, in issuing a proclamation about the Library, said: "American citizens, for whom the health of their loved ones is always a primary concern, can take great pride in their National Library of Medicine."

Mr. Chairman, for 150 years, the Library has quietly gone about the business of providing medical information to America's health professionals. Today it stands as the world's pre-eminent medical library, a tribute to the foresight of past generations of health professionals and legislators.

From a handful of books in the Surgeon General's office to a collection of 3.5 million housed in two modern buildings on the campus of the National Institutes of Health, the National Library of Medicine is an institution in which all American citizens can take pride. The last two decades, especially, have been a period of unparalleled expansion in the Library's responsibilities. A series of challenges in health communications has been met with a series of prudent and successful responses:

- Deteriorating medical libraries and their inability to meet the needs of the biomedical community led to the Congress enacting the Medical Library Assistance Act of 1965. This law not only improved the state of medical libraries but made possible the creation of a Regional Medical Library Network for disseminating biomedical information that has served the Nation well for 20 years.
- Concern with the quality of the environment led a Presidential commission to recommend a special Federal toxicology information program. This was established at the Library in 1967.
- The potential of new computer and communications technologies led the Congress to call for a major research and development program at the Library: the Lister Hill National Center for Biomedical Communications. Since 1968, this organization has played a key role in improving information services for medical research, education, and health care delivery.

- The Library's pioneering computerized medical information system--MEDLARS--went online in 1971 and now provides 3 million searches each year to some 4,000 institutions that are members of NLM's network. Later this year, we will add our 6 millionth record to the database.

The Challenge of the 80's and Beyond

There can be no doubt that the information needs of the medical profession will change dramatically in the years ahead. These changes will spring from new information generated by our national investment in research and also from the opportunities afforded us by evolving computer and communications technologies. The National Library of Medicine is today engaged in a series of activities that will allow the Library to shape, rather than be shaped by, these changes.

First, a formal 20-year plan is being developed for the Library with the assistance of panels of experts from around the Nation. These experts are ranging widely in considering how the Library should address the future: from the role of traditional collections and services, to computerized banks of actual scientific data (as opposed to bibliographic information), to Medical Informatics research and how it can influence medical education and health care. The plan will be presented to the Library's Board of Regents later this year.

Second, the Library, with the encouragement of the Congress, has embarked on an ambitious project to develop a Unified Medical Language System. The lack of a practical common terminology greatly impedes the efficient retrieval of biomedical information. The system now under development will permit a health care professional or scientist to move smoothly from one data source or file to another in order to gather information pertinent to the particular problem of a patient. The Library's effort to develop such a system is a joint one with the American Medical Association, university research groups, scientific professional societies, and Federal experts. Essential to any such integrating system is a way for the individual physician or scientist to dial directly into NLM's services. A new microcomputer interface that will do just that has already been developed and is now being made available to those who wish to have direct access to the Library's computers.

The implementation of a Unified Medical Language System would help to accelerate progress in other developments of national importance. These include the Integrated Academic Information Management System (IAIMS) and programs to improve the state of Medical Informatics. The IAIMS concept is to use computer and communications technologies to create systems in academic centers that integrate a variety of information in support of health research, education, patient care, and management. IAIMS grants are designed to produce exemplary, advanced, prototype systems at a small number of outstanding American medical centers. Several such centers have been funded and it is hoped that they will serve as models for others.

Medical Informatics, another beneficiary of the Unified Medical Language System, is a multidisciplinary research field involving the integration of computer and information sciences, medicine, engineering, and management science. This work provides the growing scientific and theoretical basis for the application of computers and automated information systems in medicine. One product of such research will be computerized systems with which human users can consult interactively, much in the same way that physicians and scientists now consult with their colleagues.

Preservation Initiative

The National Library of Medicine's primary function is its statutory responsibility to acquire and preserve library materials pertinent to medicine. Although the Library devotes significant efforts to carrying out its preservation responsibilities, the majority of library materials in existence today are works printed on high-acid content paper that is destined to disintegrate. NLM faces the inevitable loss of much of its collection unless preventive action is taken immediately. Data gathered by an NLM Preservation Planning Team show that 8.8% or 113,000 volumes in the NLM collection are so brittle that they must be copied to another medium to ensure long-term preservation of the information they contain. The remaining 91.2% of the volumes must be deacidified to prevent rapid deterioration. This is a problem faced by all large research libraries and we are optimistic that the Library of Congress may allow NLM to use its planned mass deacidification facility when that facility becomes operational in the next few years. Additional funds provided by Congress in FY 1986 will allow NLM to award a major contract for the microfilming of deteriorated materials.

Intramural Programs

Library Operations is the component responsible for NLM's basic mission--to build, maintain, and provide access to the world's largest collection of biomedical literature in support of progress in medicine and the improvement of public health. In FY 1985, the NLM added some 239,000 items to the collection and for the first time acquired a limited number of software packages. MEDLARS, NLM's computerized database system, not only provides online searching services, but produces many bibliographic publications, such as Index Medicus, a major index to 2,730 biomedical journals, and specialized literature searches on such subjects as acquired immunodeficiency syndrome (AIDS), smoking and health, and child abuse. In addition to providing access to biomedical literature through publications and online databases, NLM helps health professionals to obtain copies of documents in the collection.

The Lister Hill National Center for Biomedical Communications is the intramural research and development component of the Library. The Center is performing research in a number of promising areas. One of these is the use of optical discs for electronic document preservation. This technology affords the ability to store a wide range of material. There are some documents in which it is not suitable, but in others it's actually possible to improve the quality of its electronic images over that of the original documents. These systems have the ability for random access. Information is automatically retrieved by using existing citation databases as directories. Other areas of research include: research in knowledge representation with computer-based systems; examining methodologies for electronically organizing machine-readable databases to increase the productivity of NLM's indexing and cataloging; and developing prototype computer-assisted instructional materials for medical education.

The Toxicology Information Program (TIP) has two primary objectives: to create computerized toxicology databases and to provide toxicology information products and services to the scientific community. These services are made available through a variety of online information retrieval files, through query response, and interagency collaborative projects. Work continues on developing the microcomputer workstation that is to be used for retrieving information needed in responding to emergencies involving hazardous chemicals. Also a version of the Chemical Substances Information Network software has been developed called micro-CSIN for the use of the workstation.

Summary

The mission of the National Library of Medicine--the rapid and efficient dissemination of biomedical information--is an integral part of the research process. Without dissemination, the fruits of research have little value. The Library's innovative programs, many of which I have described for you today, exploit the latest advances in technology and information science expertise and thus assist the nation's biomedical research and health care apparatus to operate more efficiently and effectively.

Mr. Chairman, the request for the National Library of Medicine for FY 1987 is $56,408,000, an increase of $1,086,000 from the FY 1986 adjusted appropriation level. I shall be pleased to answer questions and supply additional information for the record.

LINDBERG, DR. DONALD A.B.
Director, National Library of Medicine

September 21, 1933. New York, New York

Education: A.B., Biology, Amherst College, magna cum laude, 1954; M.D., College of Physicians and Surgeons; Columbia University, 1958; Sc.D., Amherst College, (hon. caus.) 1979.

Professional History: 1984-present, Director, National Library of Medicine; 1971-1984, Director, Information Science Group, University of Missouri School of Medicine; 1969-1984, Professor of Pathology, University of Missouri School of Medicine; 1976-1980, Director, Health Services Research Center with Special Emphasis Health Care Technology Center, University of Missouri-Columbia; 1972-1973, Consultant for Health Sciences to Vice President for Academic Affairs; 1969-1971, Professor and Chairman, Department of Information Science, University of Missouri School of Library and Information Science; 1970-1971, Staff, Vice President for Academic Affairs, University of Missouri; 1967-1970, Director, Regional Medical Program Information Systems; 1968-1970, Staff, Executive Director for Health Affairs, University of Missouri; 1962-1970, Director, Medical Center Computer Program, University of Missouri; 1967-1969, Director, Missouri Regional Automated Electrocardiography System; 1966-1969, Associate Professor of Pathology, University of Missouri School of Medicine; 1963-1966, Assistant Professor of Pathology University of Missouri School of Medicine; 1962-1963, Instructor in Pathology, University of Missouri School of Medicine; 1960-1963, Director, Diagnostic Microbiology Laboratory, University of Missouri Medical Center; 1960-1962, Resident Physician in Pathology, University of Missouri School of Medicine; 1959-1960, Assistant Resident in Pathology, Columbia-Presbyterian Medical Center; 1958-1960, Assistant in Pathology, Columbia University College of Physicians and Surgeons; 1958-1959, Intern in Pathology, Columbia-Presbyterian Medical Center; June 1955-Sept. 1955, June 1954-Sept. 1954, Research Assistant to Dr. O.E. Schotte, Amherst College.

Honors: Phi Beta Kappa; Simpson Fellow of Amherst College (1954-55); Markle Scholar in Academic Medicine (1964-69).

Professional Memberships: Sigma Xi; American Society of Clinical Pathologists; College of American Pathologists (Telecommunication Network Committee, Committee on Emerging Technology); Missouri State Medical Association; American Association for Advancement of Science; Association for Computing Machines (SIGBIO); Salutis Unitas; American Association for Medical Systems and Informatics, Board of Directors; Symposium on Computer Applications in Medical Care, Board of Directors; National Board of Medical Examiners, Board Member; Washington Society for the History of Medicine; Editor: Information Methods in Medicine, Lecture Notes in Medical Informatics, and Journal of Medical Systems; National Academy of Practice in Medicine Distinguished Practitioner; Computer Science and Engineering Board, Institute of Medicine, National Academy of Science (1971-1974); U.S. Representative to International Medical Informatics Association, and Trustee (1975-1984).

STAFFING LEVELS

Chairman **Natcher**. Now, Doctor, you are requesting a staffing level of 504 for 1987. How does this compare with 1985 and 1986?

Dr. **Lindberg**. In 1984, when I joined the National Library of Medicine, we had a full-time equivalent staffing level of 544 persons. This declined the next year to 531. This year, we are issued 504.

So we have, in fact, lost approximately 7 percent over the period of two years.

MANDATORY COST INCREASES

Chairman **Natcher**. Your justification states that funds requested for intramural programs, and research management and support will not fully provide for mandatory cost increases.

How much do you need to cover full mandatory cost increases; and give us a breakdown of this amount for the record, please?

Dr. **Lindberg**. Yes, sir.

The total amount to bring us up to a current service level is approximately $2 million. If you prefer, I would give the details for the record.

Chairman **Natcher**. That will be fine.

[Information follows:]

FISCAL YEAR 1987 CURRENT SERVICES NATIONAL LIBRARY OF MEDICINE

[Dollars in thousands]

	Fiscal year 1986 sequestration	Fiscal year 1987 current services	Increase
Extramural program	$11,892	$12,264	+$372
Intramural programs:			
Library operations	25,566	26,493	+927
Lister Hill Nat'l Center for Biomedical Communications	9,042	9,338	+296
Toxicology information	3,317	3,415	+98
Total, intramural	37,925	39,246	+1,321
Research management and support	5,456	5,665	+209
Total	[1] 55,273	57,175	+1,902

[1] Equals appropriation of $57,808 thousand less $49,000 withheld for consultant services.

MAINTAINING FY 1986 INITIATIVES

Chairman **Natcher**. How much do you need for 1987 to maintain the initiatives begun in fiscal 1986 in, one, preservation of biomedical literature, and two, development of a Unified Medical Language System?

Dr. **Lindberg**. Mr. Natcher, in any event we will make every effort to carry forward the responsibility we have to provide high-quality information services to the biomedical community at the President's budget level.

In regard to the specific question you asked about the preservation report, we are approximately $200,000 below the recommended level now and we would be approximately $600,000 below that level in the subsequent year.

In the case of the Unified Medical Language System, we have plans which would allow us, were the money available, to operate at the level of $4 million. This Committee granted us $1 million in this present year and we are, in fact, carrying forward that project very nicely.

EXTRAMURAL PROGRAMS

Chairman **Natcher**. If you will, give us for the record a more detailed breakdown of funding for extramural programs shown on page 375 of the justification; include the figures, if you will, for 1985. If you would place that in the record for us, that will be fine.

Dr. **Lindberg**. Yes, sir.

[The information follows:]

NLM EXTRAMURAL PROGRAM

[Dollars in thousands]

	Fiscal year 1985 actual	Fiscal year 1986 estimate	President's budget
Medical Library Assistance:			
Integrated academic information management systems (IAIMS)	2,280	2,205	2,205
Research grants in librarianship and information science	370	365	387
Publication grants	403	389	374
Institutional training awards in medical informatics	1,091	1,107	1,177
Medical library resource grants	1,326	1,089	1,013
Reginoal medical library contracts	2,053	2,300	2,244
Subtotal medical library assistance	7,523	7,455	7,400
Medical informatics research	4,490	4,437	4,506
Total, extramural programs	12,013	11,892	11,906

Chairman **Natcher**. Mr. Conte, I yield to you at this time.

Mr. **Conte**. Thank you.

Doctor, I would like to welcome you.

Dr. **Lindberg**. Thank you, sir.

Mr. **Conte**. This is your second appearance before our Subcommittee. How is everything over at the Library? Do you like it over there?

Dr. **Lindberg**. Love it. It is a wonderful institution.

TECHNOLOGICAL ERA

Mr. **Conte**. I remember reading your justification just a few years ago when the main things you talked about were bread and butter operations of computer indexing, like MEDLARS and the Toxicology Information Program.

Now, to read your justification and statement, you are talking about Unified Medical Languages, computer-assisted instructions, medical informatics. It sounds like the Library has moved into a whole new plane of activity and become part of the new high-tech era.

Is that a fair assessment?

Dr. LINDBERG. I think that is exactly what is happening. I think the Library is extremely well-positioned to do that effectively. It has been a leader in information systems in the past and it has a very good, strong professional staff in operation and the respect of the field.

Now, I think we have to look carefully to what the next 20 years hold for us. Presently, the Board of Regents and five panels of outside experts are making a long-range plan for us. Their report will be available by year's end so we are addressing exactly the questions you mentioned.

NLM SESQUICENTENNIAL

Mr. CONTE. I notice that this is the 150th anniversary of the National Library. Do you plan to have a little celebration?

Dr. LINDBERG. Yes, sir. We think that it is, of course, a unique event and it offers the opportunity to increase the awareness of the health professions of what I consider the very good work that the institution does.

We are off to an awfully good start with the joint resolution of the Congress, thanks to your Committee and the Senate making this a sesquicentennial year of the National Library. We very much appreciate that.

It tremendously helps morale of the staff and I think it will help increase the awareness of the health professions, and the public, of what we do.

BUDGET TABLE

Mr. CONTE. As I look at your budget, I have to say I'm a little confused. In looking at our bill, I see we appropriated $57.8 million in FY 1986. But when I look at your justification tables, you keep referring to the FY 1986 appropriation before sequester of $63.2 million.

Why this disparity?

Dr. LINDBERG. Well, I think the problem is that the $63.2 million includes no-year funds for a biomedical information and comunications center at Oregon Health Sciences University amounting to $5.4 million.

Mr. CONTE. That would be a one-time shot of money.

Dr. LINDBERG. That is a one-time affair. Most of those moneys have not yet been requested nor awarded, but the project, I gather, is definitely alive. So funds are carried forward to be obligated as shown in our budget; but, in fact, they are earmarked.

FOREIGN USER CHARGES

Mr. CONTE. How are we doing in charging our foreign users the full cost of your computer tapes? Last year, you estimated you would get about $500,000, $600,000 the first year and then about $900,000 thereafter. Are you hitting those numbers?

Dr. LINDBERG. Well, Mr. Conte, I am awfully glad you asked. [Laughter.]

Mr. CONTE. Thought I never would, didn't you. [Laughter.]

Dr. LINDBERG. Well, we did estimate in that first partial year our additional billings from foreign users would be between $500,000 and $600,000; and they were $500,000.

We estimate that we would reach $900,000 in this our first full year, and will be at $1.1 million.

Mr. CONTE. Terrific.

Dr. LINDBERG. That is going very well.

OTHER USER CHARGES

Mr. CONTE. I am really pleased to hear that.

Are there any other places where you could be charging user fees or getting higher user fees for your services?

Dr. LINDBERG. There perhaps are. We are looking at one area that we think is both an opportunity of that sort and also a scientific and service opportunity. That is the provision of these various data bases or subsets thereof on the new electronic media.

There is a thing called the CD ROM. It is the little commercial diskette usually with electronic music on it, but it also can store information.

A number of commercial companies have an interest in marketing our data base in that form. We have decided that that is probably a very reasonable kind of partnership. Fundamentally they will have to spend a good bit of money in the next few years testing the marketplace.

I certainly would not come before you all and request Government funds to develop marketplaces. That is a very good opportunity to use the private sector.

Mr. CONTE. Sure.

Dr. LINDBERG. So we have signed experimental agreements with six such companies and if that goes well I think that will be an item of the sort that you mentioned. This will also be a real service to the profession because all the information will be available locally.

APPROPRIATION LANGUAGE

Mr. CONTE. That would be good.

Now, your budget calls for $20 million to be met from the collection of user fees. Last year the proposal was $15 million, and you and the Department testified that you collected only $8 million, and had no idea where they got that $15 million figure. Any change in your understanding of this year's proposal?

Dr. LINDBERG. No, sir. There really is not a change except in the numbers. This language is proposed, again, by the Administration as part of an overall policy regarding user fees.

In the particular case of NLM, we presently utilize a very satisfactory mechanism for billing and collecting MEDLARS usage charges through the National Technical Information Service of the Department of Commerce. Under this arrangement, revenues are used to pay for access costs that are not included in the NLM appropriation; and the difference between the revenues and such expenditures is returned to the U. S. Treasury.

So that authorizing language probably will not effect this, whether it says $15 million or $20 million.

Mr. CONTE. Do you still remain opposed to the idea of crediting user fees to your own account rather than turning them over to the Treasury, as your are doing at the present time? It might be a way of getting a little extra money into your budget during these tight years.

Dr. LINDBERG. Well, I think the same principle holds this year as last to be truthful, sir. I believe that we are better off the way we are doing business and returning the excess to the Treasury. I fear that it would otherwise put us into a commercial competition with those who on the private side properly operate information services.

REAUTHORIZATION LEGISLATION

Mr. CONTE. What effect does the NIH reauthorization legislation have on the Library, if any?

Dr. LINDBERG. The most important part of it for us is the Medical Library Assistance Act Reauthorization and that brings the authorized level to $12, $13, and $14 million for FY 1986, FY 1987, and FY 1988 respectively. In addition, there are some technical changes.

For example, the resource grants may be awarded up to $500,000 instead of $200,000; and that updates the number that was originally established in 1965. So those are the two most significant changes for us.

IAIMS PROGRAM

Mr. CONTE. Doctor, tell us where the IAIMS program is now. This, as we all know, is the program to set up computer network communications in some of the medical schools around the country.

Dr. LINDBERG. The basic idea of the IAIMS initiatives was to help schools that wished to integrate their information systems, bringing them together for purposes of teaching, research, and practice. Because they are competitive awards, it is possible to select distinguished schools and advanced medical centers.

The concept was to help institutions initially through the phase of planning with a relatively small amount of money and then competitively to select a slightly smaller number of schools to fund during the development phase. We are in that phase at the moment.

Between the two phases eight schools have been funded.

Mr. CONTE. Eight?

Dr. LINDBERG. Eight, sir.

In order to get to phase three, which is to build a prototype system, we would need to have a competition and applications. We could not afford to do that within the present funding level, but subsequently perhaps it will be possible.

Mr. CONTE. What is the IAIMS budget for FY 1986 and FY 1987?

Dr. LINDBERG. It is $2.2 million for the IAIMS program in each year.

Mr. CONTE. And you will use this for what?

Dr. LINDBERG. Well, some of the schools are still in the planning phase and some are in the development phase. So the awards vary.

But basically the planning is $100,000 a year and the development has been approximately $400,000 a year.

Mr. CONTE. Are any of the eight institutions ready for phase three?

Dr. LINDBERG. They will be inside of a year, but they are not ready this year.

Mr. CONTE. How about Tufts? Are they participating in the program?

Dr LINDBERG. Tufts has not yet joined that program. They have expressed an interest in it and also expressed an interest in the Centers of Excellence program.

Mr. CONTE. I saw in a notice that you were up there helping them kick off their computerized information network.

Dr. LINDBERG. That was a very exciting week.

Mr. CONTE. You sent some stuff over to China?

Dr. LINDBERG. We had what was the first interactive two-way TV with Peking. It went off absolutely flawlessly in the brand new Sackler Communications Center and Library.

PRESERVATION PLAN

Mr. CONTE. That is great.

You have provided us with a massive report on preservation of biomedical literature, "A Plan for the National Library of Medicine." Can you summarize the report for us, and are the resources called for in your report included in your budget request? If you would rather, you can do that for the record.

Dr. LINDBERG. No. I can tell you about it.

Mr. CONTE. All right.

Dr. LINDBERG. It was a very carefully done study and it has six recommendations, which I can mention very briefly.

One is the creation of a planning section: that is to say an organization in the Library to be responsible for this initiative. We have accomplished that without any additional FTEs.

Second, to establish a four-year plan for preservation microfilming. We are strong on planning in our institution. Three, to expand research in the use of electronic disk storage and to cooperate with the Library of Congress and the National Bureau of Standards, which indeed we already are.

Four, to somehow or another arrange for deacidification services for the bulk of the NLM collection. Again, we hope that we may be part of the Library of Congress operation when that gets going.

Five, to promote the use of acid-free paper. I would like, some one of these years, to be able to come before your Committee and say that we have eliminated the problem rather than just asking you for more money to keep patching up the growing problem created by printing the darn books on acid paper to begin with.

Lastly, the plan calls for developing a national plan for the preservation of the country's biomedical literature: that is to say we would like to know who is responsible for each critical element of the literature, whether we have to hold it or whether certain of the other schools and libraries will hold it.

So we are going forward with that plan. It calls for various funding levels for that four-year period. I mentioned the first at $600,000. The levels for fiscal years 1987 and 1988 would be the same at $1,200,000. In 1987 an additional $400,000 is needed for deacidification assuming that the Library of Congress can provide it and assuming that that would be the proper amount. We estimate it would be.

Mr. Conte. Very good, Doctor. I have other questions that I will submit for the record.

Thank you very much, Doctor.

Dr. Lindberg. Thank you, sir.

Chairman Natcher. Mr. Early?

HOURS OF SERVICE

Mr. Early. Thank you, Mr. Chairman.

Doctor, in reviewing your revised 1986 and your 1987 budget requests, I was concerned to see that the Library is considering a reduction in the hours of service to the public. Would you comment on that?

Dr. Lindberg. Well, it is certainly correct to say that we considered it. We considered it seriously. We costed it out both in terms of dollars and in FTEs; and the latter is even worse of a problem for us than the former.

We rejected the idea because we concluded that it is bitterly resented by the reading public, even the medical public. While we are very badly hurt on the FTEs, still we think it is one of the last things that should be done.

Mr. Early. I agree with you.

IAIMS

Dr. Lindberg, what is the status of the Integrated Academic Information Management System project?

Dr. Lindberg. It has been very, very well received by the academic community. We just had the second of the conferences at NLM for those who are interested in it, and once again an overflow audience. There were some 61 schools represented and perhaps over 200 people.

The awards have been made, as I indicated, to eight schools, some of whom are already in the second phase—development of experimental systems. So we think that the IAIMS project is going forward quite well and it does seem to answer a real need in the universities.

Mr. Early. In light of the Gramm-Rudman reductions and those in your 1987 budget request, do you think you will be on schedule with regards to the IAIMS program?

Dr. Lindberg. Well, it would not be possible to accommodate phase three within the present budget.

Mr. Early. Would you provide, for the record, much more detail on that and on the actual amount of slippage?

Dr. Lindberg. Yes.

I should say that we will, with the present budget, live up to all the commitments that we made on the IAIMS, but it will remain within the phase one and two.

Mr. **Early**. Doctor, I have several other questions which are going to call for lengthy answers so I am just going to insert them in the record. If you would answer them for the record, I would appreciate it.

Dr. **Lindberg**. Be pleased to.

Mr. **Early**. Thank you, Mr. Chairman.

Chairman **Natcher**. All right.

Mr. Hoyer?

BUDGET REDUCTIONS

Mr. **Hoyer**. Doctor, I listened to a number of the questions and maybe the questions I have have been asked.

First of all, what will we not be able to do that you think we should have done as a result of the cuts that you received from your budget request?

Dr. **Lindberg**. Well, Mr. Hoyer, as I indicated we are going to live up to all the obligations we made on the external grants and we are going to continue to provide good biomedical service.

There are a number of initiatives which the Library was prepared to take based on our original request. I guess I should mention to you the areas that those involve because they are basically the same areas that are involved in the Gramm-Rudman sequestration.

The National Library of Medicine's budget is essentially two-thirds service. So when reductions are allocated by budget activity, as we were instructed to do, naturally that means that two-thirds of the reductions are in services. Those will include reductions in the acquisition of the literature, and some delay in the indexing and some delay in the cataloging. The results of research will not appear in quite as timely a fashion as they otherwise would.

On the other hand, we hope that we will be able to do this in a selective fashion so that the most important results—let's say the side effect of drugs or improved therapies—will get done on time and something else will slip somewhere. So there will be a little bit of a backlog therefore on the processing of the literature itself.

In addition, we have allocated the reductions as follows: $535,000 in the extramural programs; the Lister Hill research activities were reduced by $407,000; and the toxicology data base systems were reduced by $149,000. So the reductions will be distributed across the areas as I indicated and as we were instructed.

Mr. **Hoyer**. Thank you, Doctor.

I have some other questions, but I know Mr. Early is going to submit some and I think they are probably duplicative. I appreciate your answer to my question.

Thank you, Mr. Chairman.

Dr. **Lindberg**. Thank you, Mr. Hoyer.

Dr. Lindberg, we want to thank you and your associates for appearing before our Committee at this time in behalf of your budget request for fiscal year 1987. It has been a good hearing, Doctor, and thank you very much.

[The following questions were submitted to be answered for the record:]

IAIMS PROGRAM

Mr. Natcher. Please describe briefly your plans for the IAIMS Program in 1986 and 1987?

Dr. Lindberg. We will continue to support the planning and development of Integrated Academic Information Management Systems (IAIMS), and to support research directly related to these efforts. Eight institutions are presently receiving grants. Total IAIMS Program funding levels are planned at $2.2 million in 1986, and the same level for 1987.

Interest in the Program remains high. A second IAIMS Symposium, sponsored by NLM in March 1986, drew even more attendees than the first one held in October 1984. More than 200 individuals, representing all levels of academic health centers, heard a day-long series of reports on IAIMS activities and the support of innovations in health sciences education.

In addition to continuing to support IAIMS activities and to encourage this important program initiative, we will also seek to take advantage of an exciting and somewhat unexpected aspect of IAIMS developments. An IAIMS activity at a health institution, besides providing a planning and development effort for establishing an institution-wide computerized integrated information network, also creates a locus for a multitude of studies and actions to improve information access and use. IAIMS sites are developing as multidisciplinary centers bringing together experts in medical informatics, knowledge organization, clinical decision systems, education and training, and health administration for unique and highly creative efforts to not only plan and research, but to implement significant advancements in the ways health professionals use information. These "spin-off" benefits provide an even greater incentive to promulgate the encouraging progress of existing awardees. Health academic institutions of every type will profit from their experiences. Thus, NLM will continue to make every effort in 1986 and 1987 to facilitate and to expand a national dialogue on the IAIMS initiative.

APPROPRIATION LANGUAGE

Mr. Natcher. You are requesting some new appropriation language. Please explain why this language is necessary or desirable.

Dr. Lindberg. This language has been proposed again this year by the Administration, as part of an overall policy regarding user charges. In the particular case of NLM, we presently utilize a very satisfactory mechanism for billing and collecting MEDLARS user charges through the National Technical Information Service of the Department of Commerce. Under this arrangement revenues are used to pay for access costs not included in the NLM appropriation. The difference between revenues and such expenditures is returned to the U.S. Treasury.

Mr. Natcher. How much money do you expect to collect in 1987 from the exchange or sale of services or material? Give us the comparable figures for 1985 and 1986.

Dr. Lindberg. We expect to collect approximately $10 million in 1987 as compared with $9.5 million in 1986 and $8.2 million in 1985. After expenditures the net amount of approximately $4 million will be returned to the Treasury.

Mr. Natcher. If this new language is approved, how would you use the funds collected?

Dr. Lindberg. If these funds were not returned to the Treasury they would be utilized for unbudgeted new program initiatives.

UNIFIED MEDICAL LANGUAGE SYSTEM

Mr. Conte. Tell us what has been happening with your top priority at the Library, which is the development of a Unified Medical Language.

Dr. Lindberg. As I indicated to you when last we discussed the Unified Medical Language, this is a very large and complicated task which will require the collaboration of Government, universities, professional societies and other elements of the private sector.

To coordinate these activities with professional societies, medical insurors, and private American organizations involved in standardizing medical terminology and nomenclature, we have established a working agreement with the American Medical Association.

To solicit the collaboration and involvement of the academic community and relevant governmental units in the necessary research and development, we are in the process of developing contractual relationships with four or five academic institutions with the resources to join us in this program.

And to develop the overall strategic plan for the implementation of this program, NLM and DCRT staff have been working to develop tools, examine certain assumptions and acquire data to define the scope, outline the alternative approaches and specify specific tasks which need to be undertaken.

Mr. Conte. How are you financing this work, and how do the FY 1986 resources compare to your funding in FY 1985?

Dr. Lindberg. Working with the American Medical Association, university investigators in academic departments, and health professional educators, NLM has initiated a coordinated program to create a Unified Medical Language.

In FY 1985 NLM obligated approximately $300,000 and we estimate spending $1,000,000 in both FY 1986 and FY 1987 for the development of the Unified Medical Language System.

BIOETHICS

Mr. Conte. Are there continuation funds included in your budget request to support the bioethics program at the Kennedy Institute?

Dr. Lindberg. Presently in FY 1986 NLM supports two awards to Georgetown University for bioethics at the Kennedy Institute. One award begun in FY 1985 is "to establish and maintain a national reference center for bioethics" and has future commitments through FY 1989. The second award is a cooperative agreement which supports the Center for Bioethics

Information. NLM has assisted Georgetown University in this endeavor since 1974. NLM has also provided support for indexing this field and making it nationally available through a printed annual, Bibliography of Bioethics, as well as a computerized bibliographic database, BIOETHICSLINE. For this latter award the period for approved funding ends in FY 1987; however, should Georgetown University choose to submit an application for a competitive renewal award, it would compete against the pool of available funds for new and competing renewal grants which is approximately $1.7 million in FY 1987.

MANDATORY COST INCREASES

Mr. Conte. With regard to your Intramural Programs and your Research Management and Support, you indicate in your justification that the budget request covers only part of the mandatory cost increases. What happens with the rest of the mandatory cost increases? Is this a problem?

Dr. Lindberg. Since we must provide funds to cover our mandatory cost increases such as inflation, we must find ways to more efficiently run our programs or reduce program efforts to offset these costs.

SALARIES

Mr. Conte. In fact, your justification seems to show a personnel cost freeze in terms of average ES salary, average GS grade and average GS salary from FY 1985 through FY 1987. Is that realistic?

Dr. Lindberg. These figures represent estimates of average personnel cost and were not intended to imply a freeze in this area. We expect salaries to increase due to within-grades and promotions, however, we estimate that these increases would be offset by other savings such as replacing personnel at lower salaries.

RESEARCH TRAINING IN MEDICAL INFORMATICS

Mr. Conte. Finally, I was intrigued to read of your new program in postdoctoral research training in the field of Medical Informatics. Who receives this type of support, and how many traineeships are you supporting?

Dr. Lindberg. NLM's support of research trainees has actually been in existence since 1972. The research initiative was previously called Computers-in-Medicine and a redirection took place in FY 1981 at which time we started to support only postdoctoral candidates in what we now call Medical Informatics. Physicians or postgraduate students in biomedical disciplines who are seeking training in the application of medical informatics are eligible to apply. The training curricula are multidisciplinary, involving medicine, the cognitive sciences, information science, and computer science. NLM is the sole federal source for this important activity. The amount budgeted for this program in both

FY 1986 and FY 1987 is approximately $1.2 million, and supports about 28 trainees. Ten years ago, in FY 1976, NLM supported 91 trainees in this field.

1986 SEQUESTRATION

Mr. Early. Under the sequestration order, the NLM budget will be reduced by $2.486 million. What effect will this reduction have on the Library's activities and operations? Will these reductions have any impact on service to the public and, if so, to what extent?

Dr. Lindberg. The National Library of Medicine will of course maintain high quality basic information services to the health community and strive to minimize the impact of the $2,486,000 reduction to our FY 1986 budget. However, since two-thirds of NLM's budget is committed to important service functions, services now must somehow be reduced. For example:

- The actual acquisition of books and other publications will need to be reduced. Literature costs continue to rise by 10-12% per year.
- NLM indexing and cataloging practices--which affect all the nation's medical libraries--will be altered which will increase the backlog of unprocessed materials. We will focus our efforts on making the most important results available.
- Support for the preservation initiative and collection maintenance will be reduced below optimal levels. Approximately 113,000 volumes in our collection are severely embrittled and this number is increasing.

Extramural Programs will be reduced by $535,000 which represents a $295,000 reduction in the IAIMS program and a $199,000 reduction in Medical Informatics research. Fewer new and competing awards will be made and in some instances noncompeting grant commitments will be negotiated downward.

The Lister Hill Center's research and development programs will be reduced by $407,000. The Toxicology Information Program's decrease of $149,000 will have a serious effect on the Library's ability to maintain and enhance toxicological databases. Reduced Superfund support in FY 1986 has already harmed these efforts.

The Research Management and Support activity will decrease by $245,000. Travel, other administrative costs, and staffing levels will be reduced.

UNIFIED MEDICAL LANGUAGE SYSTEM

Mr. Early. Doctor, what is the status of NLM's project to develop a uniform medical language system?

Dr. Lindberg. One of the most serious deficits faced by health professionals in retrieving information is the lack of a practical unified medical language system that would permit communication between the many and varied health information systems. A study was undertaken by NLM staff in FY 1985 to determine the feasibility of developing a Unified Medical Language System. With this study, the encouragement of outside research groups who were consulted, and a Congressional increase in FY 1986, NLM is now proceeding with the development of such a system.

Mr. Early. What activities do you have planned in this area for FY 1986 and FY 1987?

Dr. Lindberg. In FY 1986 we intend to define the basic assumptions which will underly the initial design efforts. Among these, with regard to the clinical record vs. the medical literature, are the following: to what extent are the words, abbreviations, and jargon of the clinical record unique to the clinical record? Is the difference in word usage in Clinical Record structure and Medical Subject Headings structure a matter of specificity or altered meaning? Are direct maps between numerous medical information structures feasible or is mapping to a common, even if artificial structure, the best strategy? Preliminary studies have already given us insight into these questions and by the end of FY 1986 NLM will be in a position to begin more specific studies which will be addressed in FY 1987. Among these are:

1. Systematic analysis of the relationship between the language used in clinical patient records and that used in the NLM thesaurus and that used in the scientific literature.

2. Systematic analysis of the relationship and possible mutual complementarity between the NLM thesaurus, and thesauri and nomenclature supported by selected professional associations.

In order to pursue effectively these questions, NLM will establish contractual relationships to support joint and coordinated research and development between NLM and the university-based and private sector-based organizations that have the interest and ability to contribute to this project.

In addition, in FY 1987 we look forward to the creation of the initial tools with which to construct the System.

1987 BUDGET SUBMISSION

Mr. Early. What activities did NLM propose in its budget submission to NIH that it will now have to forego?

Dr. Lindberg. The original FY 1987 NLM budget request was for $77.7 million. Compared to the President's request of $56.4 million our original request provided for these additional activities:

- IAIMS program could accelerate the developmental phase and begin the third stage--implementation of prototypes.

- A comprehensive Centers of Excellence in Medical Informatics program would be initiated.
- Funding for investigator-initiated projects and training of researchers in Medical Informatics would more than double.
- An additional 77 FTEs were requested.
- NLM would significantly expand its program to create a Unified Medical Language system.
- The literature acquisitions budget would be restored to an optimal level, as would cataloging activities and preservation programs.
- Research in artificial intelligence and expert computerized consultation systems would be accelerated.

NLM'S COLLECTION

Mr. Early. What is the status of NLM's collection activities? Any problems in this area or are things going smoothly?

Dr. Lindberg. NLM continues to acquire substantive biomedical books, journals, and audiovisual materials from around the world and to add to its important historical collections of rare books, prints and photographs, and manuscripts. Over the past year, the Library has begun to acquire a limited number of biomedical software packages and is determining the costs of acquiring, cataloging, and making these items available for onsite use. Having completed a major review and revision of its guidelines for selecting items for the collection in 1985, NLM has now embarked on a series of projects to evaluate the strength of its collection in specific subject areas. The annual production of biomedical literature that falls within the scope of the NLM collection continues to increase; the per unit cost also increases at a rate substantially above general inflation. For the last few years, the strength of the U. S. dollar has counteracted the combined effects of increased publication activity and inflation to a certain degree. The current decline of the dollar naturally increases the funds necessary to purchase foreign literature and strains the Library's ability to keep pace with current publication activity, particularly at a time when publication of biomedical information in new electronic formats is growing dramatically.

Mr. Early. Will the FY 1986 Gramm-Rudman reductions have any adverse impact on this area? What aspects of the library's collections activities will be affected and how?

Dr Lindberg. There will be a reduction in the amount available for acquisition of literature. Although the number of volumes added to the collection will be reduced, we will attempt to collect the most important information so as to minimize the impact upon the biomedical community. Also NLM will reduce its planned acquisitions of biomedical software.

LIBRARY OPERATIONS

Mr. Early. The justification indicates that under the FY 1987 request acquisition of the literature, cataloging, and indexing would be performed at a reduced level. From what level are you reducing - the FY 1986 revised level, FY 1985, or is there a recommended level/standard that NLM tries to meet each year?

Dr. Lindberg. There will be an effective reduction from all three of those levels. The FY 1987 request for acquisition is 2.6% higher than the FY 1986 revised budget level. The request for cataloging and indexing is approximately 2.4% higher than the FY 1986 revised budget level.

In general, NLM tries to acquire all substantive biomedical literature that falls within the scope of its collection. The 2.6% increase will not support this acquisition level because the estimated FY 1987 inflation rate for current biomedical literature is 10%. The continuing decline of the dollar could also reduce NLM's purchasing power substantially. NLM's desired goal for cataloging is to handle all incoming materials as they are received and to reduce the cataloging backlog which has developed over the years. Unfortunately the cataloging backlog will increase in FY 1987 and some cataloging records normally provided to the nation's medical libraries will not be available. The current goal for indexing is to process about 300,000 articles per year and maintain goals for throughput time, which will be difficult to achieve.

Mr. Early. Will acquisition of literature, etc., be at the level it should be in FY 1987 in light of this budget request?

Dr. Lindberg. NLM will attempt to set priorities and acquire, catalog, and index the most important items from the literature that would normally be acquired and processed. At the FY 1987 request level, some items that fall within the scope of the NLM collection will not be acquired, the cataloging backlog will grow, and an indexing backlog will develop.

Mr. Early. Generally what is the effect if you lag or fall behind in this area?

Dr. Lindberg. The general effect is to reduce access to portions of the biomedical literature for U. S. health professionals. Because NLM under its statutory mandate acquires many items not purchased by other U.S. libraries, a reduction in NLM literature acquisitions may mean that certain items will not be available in any library in the country. It should be recognized that because some publishers produce very limited numbers of scholarly works, it may not be possible to go back and purchase items published earlier when funds become available. Increased backlogs of cataloging and indexing mean that some items of potential importance will not be announced to the U.S. biomedical community in a timely manner. NLM will attempt to set priorities so the most critical items continue to be purchased and processed expeditiously.

Mr. Early. What standards has NLM established for cataloging and indexing? What kind of turnaround time do you shoot for?

Dr. Lindberg. The standards vary depending on the materials being handled. The intent is to process materials that are likely to receive the greatest use as quickly as possible. In cataloging, pre-publication galley proofs receive the highest priority because publishers are waiting for the cataloging data so that it can be published right in the book. The throughput goal for this material (which constitutes about one quarter of the monograph cataloging workload) is 48 hours. The goal for high priority English language books (another quarter of the workload) is five to six weeks. Goals for turnaround time for cataloging other materials vary based on language and format. In indexing, the goal is to index and announce high priority English articles (about 25% of the total) within 4 weeks. The goal for the remainder is 8 weeks.

Mr. Early. Doctor, is there a backlog in cataloging and indexing. If so, what is the extent of the backlog?

Dr. Lindberg. There is a backlog in cataloging of about 15,000 items, which represents more than a year's workload. There is currently no backlog in indexing, although at any given time there may be two to three weeks work at various stages in the indexing process.

Mr. Early. Will it decline or grow given your FY 1987 budget request.

Dr. Lindberg. The cataloging backlog will grow, and an indexing backlog will probably develop.

Mr. Early. Doctor, what are you allocating in FY 1986 and FY 1987 for collection activities? How does this compare to FY 1985 expenditures in this area.

Dr. Lindberg. The allocations for acquisition of materials for the three years are as follows:

FY 1985	FY 1986	FY 1987
$2,129,000	$2,120,000	$2,175,000

The FY 1986 allocation is 0.4% below the FY 1985 level. The FY 1987 allocation is 2.6% above the FY 1986 level.

PRESERVATION

Mr. Early. I see from the justifications that NLM has developed a preservation plan for its acquisitions. Would you briefly summarize the major aspects of this plan and tell us the projected target date for completion of each component.

Dr. Lindberg. The major activities outlined in the preservation plan are listed below with their target dates.

Activities	Target Date
A. Modify NLM Board of Regents policy on preservation	Completed February 1986
B. Establish a new organizational unit to direct NLM's preservation program	Completed March 1986
C. Microfilm severely embrittled books and journal volumes under 4-year contract (initiated in FY 1986)	June 1990
D. Deacidify all materials in the NLM collection that would benefit from this treatment (to begin in FY 1989)	2005
E. Expand efforts to preserve items now in the special historical collections (initiated in FY 1985)	June 1990
F. Continue research on the preservation characteristics of optical disk	Ongoing
G. Encourage publication of biomedical literature in archival formats	Ongoing
H. Initiate and participate in cooperative programs for preservation of the biomedical literature	Ongoing

Mr. Early. How much have you allocated for this program in FY 1986? In FY 1987?

Dr. Lindberg. In both years, the allocation for the expanded preservation initiative is $600,000, to be used for microfilming brittle volumes and preserving special collections. This figure is in addition to continuing expenditures for binding new journal issues and other recurring collection maintenance activities.

Mr. Early. How much was spent on preservation activities in FY 1985?

Dr. Lindberg. The 1985 expenditure was $200,000 for preservation of historical materials in the special collections (e.g., rare books, pictures, manuscripts). This excludes continuing expenditures for binding and other recurring collection maintenance activities.

Mr. Early. Will the FY 1987 budget request allow you to meet the timetable envisioned for this plan? If not, to what extent will there be slippage and in what areas?

Dr. Lindberg. No. The FY 1987 budget request will cause some delays in meeting preservation objectives, particularly for microfilming brittle books. The plan called for $1,200,000 in preservation expenditures in FY 1987. At the rate of expenditure in the FY 1987 request, the microfilming project will take nine years, as opposed to the four years originally planned.

TECHNOLOGY ADVANCEMENTS

Mr. Early. I see from the justification that NLM has created an in-house capability to develop artificial intelligence systems. Tell us about this program, and why it is important to NLM's mission? When was it established? What are its goals?

Dr. Lindberg. New advances in computer systems and software technology have provided the National Library of Medicine (NLM) opportunities to explore the development of new and more efficient ways to provide information to the health care community. Paramount among these new opportunities is the application of artificial intelligence systems. In 1984, NLM started two programs which utilize artificial intelligence techniques; a program in the use of expert systems and a program in automated indexing.

The expert systems program combines the use of knowledge-based systems, which are more complete than the traditional bibliographic data base systems, with machine-based searching techniques that emulate human reasoning processes. The goal is to provide medical practitioners diagnostic and patient management support in the clinical setting.

Research in automated indexing is pursued to develop more efficient methods of identifying, representing, and retrieving relevant information from medical documents. Each year, expert indexers at the National Library of Medicine manually index and add approximately 300,000 citations to MEDLINE, NLM's computerized bibliographic database. MEDLINE is available for searching at over 4,000 locations across the country. The automated indexing program is concerned with exploring research areas that will ultimately aid both in the indexing and retrieval of this vast amount of information.

Both research programs are directed towards the Library's goal to provide medical information in an efficient and useful format to health care providers.

Mr. Early. Doctor, there have been numerous advances in technology--in the field of computer technology, electronics optics. I suspect that these advances are changing what the Library looks like and how it carries out its missions. What have been some of the most dramatic changes in the past few years?

Dr. Lindberg. Yes, advances in technology are changing both how the Library looks and how it is carrying out its mandate. Probably one of the most dramatic changes in the Library has been the removal of the traditional card catalog that generations of biomedical researchers have used in search of references. In its place, the biomedical researcher has greatly improved access via easy-to-use computer terminals. Not as dramatically apparent, but of similar purpose, the Library has made available a personal computer based program, Grateful Med, to allow the biomedical researchers and practitioners easy, direct access to the journal literature citations in MEDLINE from their own offices or homes. Existing access to MEDLINE via the sophisticated ELHILL Retrieval System has been very effective for librarian intermediaries, but we have been striving to improve the system in order to bring the information directly and more effectively to the health science users themselves.

Inside the Library, but unseen by most users, the deployment of a Local Area Network (LAN) for both broadband (video) and data, coupled with improved personal workstations in critical areas, has allowed the library to improve services beyond that which would have been possible without these technologies.

A dramatic new technology for computer storage, the optical disk, is currently being evaluated as a means of providing still another way, in combination with the growing availability of personal computers, to disseminate the information products of the Library. One compact disk (CD-ROM), 12 cm (4.7 in.) in diameter, will be able to store about one full year of journal citations from MEDLINE, or our entire electronic "card catalog" of monographs and journal titles.

NLM is currently engaged in a number of experimental projects in this area with the private sector. In the future, we look forward to utilizing the optical disk storage technology to maintain improved archival records of our collection. We have a research program, the Electronic Document Storage and Retrieval System (EDSR), directed toward this goal. Questions remain to be answered regarding the most effective use of the optical storage technologies, but we are actively investigating them.

The optical videodisc technology is already being exploited in various places in the Library. Our History of

Medicine Division has created a videodisc catalog of pictures from our very extensive and valuable picture collection. We have, as a result, been able to make this disc available to educational and other health science institutions throughout the world. Prior to this technology, it was simply not practically feasible to make access to this collection so broadly available. The optical videodisc is finding extensive applications in research programs in our Lister Hill Center for Biomedical Communications in the areas of computer-based education, clinical case simulations, differential diagnostic aids, and expert systems. Many of these research efforts are regularly demonstrated to members of the health sciences community in our National Learning Demonstration Center (NLDC), where exemplary items in computer-based education from outside the Library are also displayed.

This is a very brief overview of how advances in technology are changing the way library looks and how it is performing its mission of improving biomedical communication.

RESEARCH AND PLANNING

Mr. Early. Doctor, what kind of research and planning is the NLM doing to accommodate all this new technology? To evaluate what would be beneficial to the library's mission?

Dr. Lindberg. The revolution in information management effected by computer and communication technology has created enormous challenges. To ensure these challenges are met, the NLM Board of Regents has embarked on a long-range planning process for NLM that, in addition to producing a blueprint for the future, is serving as a sounding board for the varied constituencies to advise the Library about the direction of its programs.

Mr. Early. Do you have a master plan dealing with this matter or are you developing one?

Dr. Lindberg. With the assistance of five distinguished panels of experts, the Library is developing a long-range plan. This plan, which I will be able to present to you at next year's hearing, will be a blueprint for the Library's programs and activities for the next 20 years. In this way, we expect to meet the challenge of changing information needs and technologies.

Mr. Early. What resources is NLM allocating to this area and are these resources sufficient to keep abreast of things?

Dr. Lindberg. NLM has adequate resources to develop this initial plan with the assistance of outside experts. For such a plan to be useful and up-to-date expert consultants will need to be utilized on a regular basis.

FTE REDUCTION

Mr. Early. To what extent will the proposed reduction in FTEs (-14) affect NLM's operations? In what areas will these decreases be made?

Dr. Lindberg. When one compares this year's ceiling of 504 to the FY 1985 FTE usage of 531 it constitutes a reduction of 27 FTEs. Since NLM is primarily a service oriented institution, such reductions are harder to absorb than for most institutions. Although we will strive to minimize the impact on library services, a reduction of this magnitude imposes serious constraints on the Library's ability to effectively provide high quality biomedical information services to the health community.

No longer can technological advancements buffer reductions as they have in the past. NLM will need to consider carefully its options to alleviate the impact of these staff reductions upon basic library functions.

IAIMS

Mr. Early. How many grants will have been made by the close of FY 1986?

Dr. Lindberg. We have not finished making all our FY 1986 competitive awards, so I cannot answer your question at this time. However, to date, we have supported IAIMS planning and/or development at eight institutions.

Mr. Early. Are you planning any new awards for FY 1987, and if so, how much have you budgeted for new awards?

Dr. Lindberg. In FY 1987 we have budgeted approximately $200,000 for new awards.

Mr. Early. Last year, you indicated that you hoped to be able to make some development phase awards. Have you been able to do so?

Dr. Lindberg. In FY 1985 we awarded 4 developmental awards.

Mr. Early. Are you planning any development phase awards for FY 1987?

Dr. Lindberg. In FY 1987 we have allocated $1,205,000 for development phase awards.

Mr. Early. Is it still your goal to fund four or five projects through the final completion of the prototype?

Dr. Lindberg. Yes.

Mr. Early. What resources are being allocated to the IAIMS program in FY 1986 and in FY 1987.

Dr. Lindberg. In FY 1986 and FY 1987 we plan to allocate $2,205,000 to the IAIMS program.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

National Library of Medicine

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National Library of Medicine

For carrying out section 301 *and Title IV of the Public Health Service Act* with respect to health information communications [and part I of title III of the Public Health Service Act, $57,956,000], *$56,408,000 together with not to exceed $20,000,000 to be derived from the exchange or sale of services or materials as authorized by section 382 of the Public Health Service Act. (Department of Health and Human Services Appropriation Act, 1986.)*

National Library of Medicine

Language Analysis

Language Provision	Explanation
..."together with not to exceed $20 million to be derived from the exchange or sale of services or materials as authorized by Section 382 of the Public Health Service Act.	The proposed language would authorize the National Library of Medicine to utilize for general operating costs of the Library up to $20 million generated through sales and exchanges of services and materials.

NATIONAL INSTITUTES OF HEALTH

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Amounts Available for Obligation 1/

	1985	1986	1987
Appropriation	$55,910,000	$57,956,000	$56,408,000
Enacted administrative reduction	—	-148,000	—
Sequester order	—	-2,486,000	—
Proposed rescission	—	—	—
Subtotal, adjusted appropriation	$55,910,000	$55,322,000	$56,408,000
Real transfer to:			
Office of the Assistant Secretary for Health, for AIDS Projects	—	—	—
Comparative transfer to:			
Office of the Assistant Secretary for Health, for AIDS Projects	—	—	—
Division of Research Resources for changes in the Central Services financing mechanisms and formulas	-1,086,000	—	—
Subtotal, adjusted budget authority	54,824,000	55,322,000	56,408,000
Unobligated balance start of year	5,405,000	5,405,000	—
Unobligated balance end of year	-5,405,000	—	—
Unobligated balance, lapsing	-726,000	-49,000	—
Total, obligations	54,098,000	60,678,000	56,408,000

1/ Excludes the following amounts for reimbursable activities carried out by this account: 1985—$1,914,000; 1986—$2,439,000; 1987—$4,811,000.

National Library of Medicine

Budget Mechanism
(Dollars in Thousands)

	1986 1/ Appropriation		1986 1/ 2/ Available after Sequestering		1986 1/ 2/ Revised		1987 Estimate	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Extramural Programs								
Grants								
Noncompeting.....	55	$7,445	55	7,445	55	7,445	57	$7,785
Competing........	39	2,681	36	2,147	36	2,147	32	1,877
Subtotal, Grants.	94	10,126	91	9,592	91	9,592	89	9,662
Contracts								
Noncompeting.....	8	7,705	8	7,705	8	7,705	7	2,244
Competing........	---	---	---	---	---	---	---	---
Subtotal, Contracts.......	8	7,705	8	7,705	8	7,705	7	2,244
Total, Extramural......	102	17,831	99	17,297	99	17,297	96	11,906
					FTEs		FTEs	
Intramural Programs								
Library Operations.		26,746		25,566	304	25,566	304	26,166
Lister Hill Nat'l Center for Biomedical Communications............		9,459		9,042	78	9,042	78	9,259
Toxicology Information.............		3,470		3,317	31	3,317	31	3,470
Total, Intramural......		39,675		37,925	413	37,925	413	38,895
Research Management and Support..........		5,707		5,456	91	5,456	91	5,607
Total............		63,213		60,678	504	60,678	504	56,408

1/ Reflects an enacted administrative reduction of $148,000, and a carryover in unobligated funds of $5,405,000.

2/ Reflects a consultant services (Section 515 of the Treasury Postal Service Appropriation Act, 1985) withholding of $49,000.

NATIONAL INSTITUTES OF HEALTH

National Library of Medicine

CROSSWALK - 1986 Appropriation

Program Activity	Mechanism: Extramural Programs: Grants	Mechanism: Extramural Programs: Contracts	Mechanism: Intramural Programs	Mechanism: Research Mgmt. and Support	Total
Extramural Programs					
Medical Library Assistance.......	$5,490,000	$7,705,000	---	---	$13,195,000
Medical Informatics..............	4,636,000	---	---	---	4,636,000
Total, Extramural..............	10,126,000	7,705,000	---	---	17,831,000
Intramural Programs					
Library Operations...............	---	---	$26,746,000	---	26,746,000
Lister Hill National Center for Biomedical Communications........	---	---	9,459,000	---	9,459,000
Toxicology Information...........	---	---	3,470,000	---	3,470,000
Total, Intramural..............	---	---	39,675,000	---	39,675,000
Research Management and Support....	---	---	---	$5,707,000	5,707,000
Total..................	10,126,000	7,705,000	39,675,000	5,707,000	63,213,000

NATIONAL INSTITUTES OF HEALTH

National Library of Medicine

CROSSWALK - 1986 Available After Sequestering
and
1986 Revised Request

Program Activity	Mechanism: Extramural Programs: Grants	Mechanism: Extramural Programs: Contracts	Mechanism: Intramural Programs	Mechanism: Research Mgmt. and Support	Total
Extramural Programs					
Medical Library Assistance.......	$5,155,000	$7,705,000	---	---	$12,860,000
Medical Informatics..............	4,437,000	---	---	---	4,437,000
Total, Extramural..............	9,592,000	7,705,000	---	---	17,297,000
Intramural Programs					
Library Operations................	---	---	$25,566,000	---	25,566,000
Lister Hill National Center for Biomedical Communications........	---	---	9,042,000	---	9,042,000
Toxicology Information...........	---	---	3,317,000	---	3,317,000
Total, Intramural..............	---	---	37,925,000	---	37,925,000
Research Management and Support....	---	---	---	$5,456,000	5,456,000
Total..................	9,592,000	7,705,000	37,925,000	5,456,000	60,678,000

NATIONAL INSTITUTES OF HEALTH

National Library of Medicine

CROSSWALK - 1987 Congressional Justification

Program Activity	Mechanism				
	Extramural Programs		Intramural Programs	Research Mgmt. and Support	Total
	Grants	Contracts			
Extramural Programs					
Medical Library Assistance.......	$5,156,000	$2,244,000	---	---	$7,400,000
Medical Informatics..............	4,506,000	---	---	---	4,506,000
Total, Extramural..............	9,662,000	2,244,000	---	---	11,906,000
Intramural Programs					
Library Operations...............	---	---	$26,166,000	---	26,166,000
Lister Hill National Center for Biomedical Communications........	---	---	9,259,000	---	9,259,000
Toxicology Information...........	---	---	3,470,000	---	3,470,000
Total, Intramural..............	---	---	38,895,000	---	38,895,000
Research Management and Support....	---	---	---	$5,607,000	5,607,000
Total...................	9,662,000	2,244,000	38,895,000	5,607,000	56,408,000

National Library of Medicine

Summary of Changes

1986 Current estimated obligations.............................	$60,678,000
1987 Estimated obligations.....................................	56,408,000
Net Change..	-4,270,000

	1986 Base	Change from Base
Increases:		
A. Built-in:		
1. Within-grade increases.......	$19,000,000	+$223,000
2. Federal Employees Compensation Fund increase.......	78,000	+22,000
3. Unemployment compensation increase..................	54,000	—
4. FTS rate increase............		+63,000
5. Payment for centrally furnished services.........	4,488,000	+229,000
6. Increased cost of laboratory supplies, materials, literature, and other expenses..................	22,193,000	+878,000
Subtotal....................		+1,415,000
B. Program:		
1. Grants:		
a. Noncompeting continuations converting from competing status.......	7,445,000	+1,954,000
b. Competing (new, renewals and supplementals).....	2,147,000	+1,891,000
Subtotal.................		+3,845,000
Total increases..........		+5,260,000

Summary of Changes — continued

	1986 Base	Change from Base
Decreases:		
A. Built-in:		---
B. Program:		
1. Grants:		
a. Noncompeting completed or converting to competing status.......	7,445,000	-1,514,000
b. Competing completed or converting to non-competing status.......	2,147,000	-2,147,000
c. Indirect cost reduction..	9,592,000	-114,000
Subtotal...............		-3,775,000
2. Contracts:		
a. Noncompeting completed...	5,405,000	-5,405,000
b. Indirect cost reduction..	2,300,000	-56,000
Subtotal...............		-5,461,000
3. Intramural: Program decrease in low priority areas.......	37,925,000	-241,000
4. Research Management and Support: Program decrease in low priority areas.......	5,456,000	-53,000
Subtotal...............		-294,000
Total decreases..............		-9,530,000
Total, net change............		-4,270,000

National Library of Medicine

Budget Authority by Activity
(Dollars in Thousands)

	1986 Appropriation	1986 Available after Sequestering	1986 Revised		1987 Estimate	
	Amount	Amount	FTEs	Amount	FTEs	Amount
Extramural Programs...	$17,831	$17,297	---	$17,297	---	$11,906
Intramural Programs						
Library Operations..	26,746	25,566	304	25,566	304	26,166
Lister Hill Nat'l Center for Biomedical Communications..............	9,459	9,042	78	9,042	78	9,259
Toxicology Information........	3,470	3,317	31	3,317	31	3,470
Total, Intramural..	39,675	37,925	413	37,925	413	38,895
Research Management and Support..........	5,707	5,456	91	5,456	91	5,607
Total obligations..	63,213	60,678	504	60,678	504	56,408
Unobligated balance start-of-year........	-5,405	-5,405		-5,405	---	---
Unobligated balance end-of-year..........	---	---		---	---	---
Unobligated balance lapsing..............	---	49		49	---	---
Total budget authority............	57,808	55,322	504	55,322	504	56,408

NOTE: All 1986 columns reflect an enacted administrative reduction of $148,000, and a carryover in unobligated funds of $5,405,000.

National Library of Medicine

Obligations by Object

	1985 Actual	1986 Estimate	1987 Estimate
Total number of full-time permanent positions................	495	495	495
Total compensable workyears:			
Full-time equivalent employment....	559	532	532
Full-time equivalent of overtime and holiday hours................	7	7	7
Average ES salary....................	$66,232	$66,232	$66,232
Average GS grade.....................	9.14	9.14	9.14
Average GS salary....................	28,224	28,224	28,224
Average salary, grades est. by act of July 1, 1944 (42 U.S.C. 207).......	35,361	35,361	35,361
Average salary of ungraded positions...........................	23,206	23,206	23,206
Personnel compensation:			
Permanent positions................	$15,221,000	$14,968,000	$15,358,000
Positions other than permanent.....	1,725,000	1,697,000	1,741,000
Other personnel compensation.......	324,000	317,000	326,000
Special personal services payments.	13,000	14,000	14,000
Subtotal, personnel compensation.	17,283,000	16,996,000	17,439,000
Personnel benefits..................	2,001,000	1,954,000	2,006,000
Benefits for former personnel........	42,000	50,000	50,000
Travel and transportation of persons.	223,000	248,000	255,000
Transportation of things............	108,000	108,000	111,000
Rent, communications and utilities...	1,056,000	1,018,000	1,045,000
Printing and reproduction............	909,000	847,000	869,000

Obligations by Object

	1985 Actual	1986 Estimate	1987 Estimate
Other services:			
Project contracts...............	7,441,000	15,259,000	9,872,000
Centrally furnished services....	4,331,000	4,488,000	4,717,000
Standard level user charge......	534,000	—	—
Other..........................	3,770,000	3,681,000	3,777,000
Supplies and materials...........	498,000	462,000	474,000
Equipment........................	3,873,000	3,855,000	3,956,000
Literature........................	2,129,000	2,120,000	2,175,000
Grants, subsidies & contributions	9,900,000	9,592,000	9,662,000
Total..................	54,098,000	60,678,000	56,408,000

National Library of Medicine

Significant Item in House Appropriations Committee Report

Item	Action Taken or to be Taken
Preservation of the Biomedical Literature The Committee is particularly concerned about the preservation of the Library's collection, and requests a report on the subject including funding requirements, prior to next year's hearings. (p. 79)	The report will be submitted to the Committee prior to the hearings, as requested.

NATIONAL INSTITUTES OF HEALTH
National Library of Medicine

Authorizing Legislation

	PHS Act/ Other Citation	U.S. Code Citation	1986 Amt. Authorized	1986 Current Estimate	1987 Amt. Authorized	1987 Estimate
Research and Investigation........................	Title III, Part A Section 301	42§241	Indefinite	$4,636,000	Indefinite	$4,506,000
National Library of Medicine....................	Title IV, Part D Section 465-467	42§286	Indefinite	45,382,000	Indefinite	44,502,000
Medical Library Assistance.................	Title IV, Part D Section 469-477	42§286b	$12,000,000	13,195,000 1/	$13,000,000	7,400,000
Total Budget Authority.....				$63,213,000		$56,408,000

1/ Includes $5,405,000 in no-year funds.

National Library of Medicine

Appropriations History

Year	Budget Estimate To Congress	House Allowance	Senate Allowance	Appropriation 1/
1978	37,644,000	37,619,000	37,619,000	37,619,000
1979	39,774,000	39,887,000	42,987,000	41,431,000
1980	42,088,000	42,431,000	44,000,000	43,979,000
1981	45,188,000	44,730,000	44,569,000	44,666,000
1982	41,956,000 2/	46,252,000	46,677,000	45,035,000
1983	46,043,000	46,043,000	51,943,000	51,943,000
1984	49,616,000	42,263,000 3/	41,963,000 3/	49,613,000
1985	51,320,000	43,820,000 3/	53,500,000 4/	54,824,000
1985 Proposed Rescission	-354,000			
1986	53,320,000	46,972,000 3/	60,000,000	57,808,000
1986 Sequester	-2,486,000			
1987	56,408,000			

1/ Reflects enacted supplementals, rescissions and reappropriations.

2/ Reflects the September amendment; the original request was $47,677,000.

3/ Excludes funds for Medical Library Assistance Act programs not considered.

4/ Includes $7,500,000 for Medical Library Assistance Act programs under the Continuing Resolution. Does not include $607,000 transfer of unobligated balances from the Health Resources and Services Administration.

National Library of Medicine

Justification

	1986 Appropriation Amount	1986 Available after Sequestering Amount	1986 Revised FTEs	1986 Revised Amount	1987 Estimate FTEs	1987 Estimate Amount
Extramural Programs						
Medical Library Assistance........	$13,195,000	$12,860,000	—	$12,860,000	—	$7,400,000
Medical Informatics..............	4,636,000	4,437,000	—	4,437,000	—	4,506,000
Total, Extramural.	17,831,000	17,297,000	—	17,297,000	—	11,906,000
Intramural Programs						
Library Operations.	26,746,000	25,566,000	304	25,566,000	304	26,166,000
Lister Hill Center.	9,459,000	9,042,000	78	9,042,000	78	9,259,000
Toxicology Information............	3,470,000	3,317,000	31	3,317,000	31	3,470,000
Total, Intramural.	39,675,000	37,925,000	413	37,925,000	413	38,895,000
Research Management and Support.........	5,707,000	5,456,000	91	5,456,000	91	5,607,000
Total............	63,213,000	60,678,000	504	60,678,000	504	56,408,000

General Statement

The National Library of Medicine is the nation's primary resource for biomedical literature and for the development of biomedical information technology. The NLM's program activities and major functions are:

- o Extramural Programs - This activity funds several grant and contract programs which are designed to develop better information services for American health professionals and biomedical scientists. Major components include Medical Library Assistance programs, NLM's initiative to develop Integrated Academic Information Management Systems (IAIMS), and research in Medical Informatics.

- Intramural programs and services - These include the following activities:

    Library Operations - This national resource acquires, organizes, and maintains the Library's archival and reference collection of biomedical literature. It also provides access to that collection through a nationwide online computerized bibliographic retrieval service.

    Lister Hill National Center for Biomedical Communications - This research and development component of the Library is responsible for exploring the application of advances made in the fields of computer and communications technology to health information handling, processing and transfer problems, and to health sciences education.

    Toxicology Information - This activity develops and maintains specialized online databases on drugs and chemicals toxic to man. It collects and organizes toxicology data from the files of collaborating organizations, prepares and publishes bibliographies and reports, and operates online files.

- Research Management and Support - This activity provides the overall executive direction and administrative management necessary for the effective operation of all NLM activities, including extramural grant and contract programs.

The National Library of Medicine is the world's largest research library in a single scientific and professional field: The Library collects materials exhaustively in all major areas of the health sciences and to a lesser degree in such areas as chemistry, physics, botany, and zoology. The collections today stand at 3.5 million items—books, journals, technical reports, manuscripts, microfilms, and pictorial materials. Housed in the Library is one of the world's finest medical history collections of old (pre-1871) and rare medical texts, manuscripts, and incunabula.

The tremendous volume of scientific literature resulting from society's heavy investment in biomedical research would be of limited utility without the classifying, announcing, and distributing activities of the National Library of Medicine. The unending cycle of research, publication, announcement, and review constitutes the critical function of the biomedical information exchange network which makes it possible for medical advances to be applied to patient care.

The Library was a pioneer in developing computerized bibliographic retrieval systems and today its MEDLARS system (Medical Literature Analysis and Retrieval System) stands as the preeminent such system in the field of medicine. MEDLARS make available for online searching more than 5 million references to journal articles, records to some 600,000 books, and citations to 14,000 audiovisual items. MEDLARS is also used to prepare for publication a wide array of bibliographies, catalogs, and indexes. The most well known of these publications is the widely consulted *Index Medicus*, in continuous publication since 1879.

Overall Budget Policy

The FY 1987 request of $56,408,000 reflects a decrease of $4,270,000 below the FY 1986 revised estimate. This decrease represents: a reduction of $55,000 for Medical Library Assistance Act programs; an increase of $69,000 for Medical Informatics research; an increase of $1,121,000 for intramural programs and research management and support activities; and $5,405,000 (the remaining unobligated balance) in no-year funds for a Biomedical Information and Communications Center at the Oregon Health Sciences University presently estimated for obligation in FY 1986. The increase for intramural programs and research management and support would offset a portion of the mandatory cost increases, which are not fully provided for at the FY 1987 level. The FTE levels at both the FY 1986 revised estimate and the FY 1987 budget request reflect a decrease of 14 FTE's below the FY 1986 appropriation level.

At the request level, the Library would continue to provide information services to the nation's biomedical community. Hours of service to the public and timeliness of availability of the latest research results in NLM's computerized databases would be maintained to the best of our ability. Acquisition of literature, cataloging, and indexing would be performed at a reduced level. Major initiatives begun in FY 1986 in preservation of the biomedical literature and development of a Unified Medical Language System would be continued at a reduced level. Within the Extramural Programs, pre-existing commitments for noncompeting grants and contracts will be honored, and some support for new and competing grant awards in each of the different mechanisms will be provided.

Program Accomplishments

The revolution in information management effected by computer and communication technology has created enormous challenges. To ensure these challenges are met, the NLM Board of Regents has embarked on a long range planning process for NLM that, in addition to producing a blueprint for the future, is serving as a sounding board for the varied constituencies to advise the Library about the direction of its programs. Planning panels composed of experts from around the nation have been convened and are developing recommendations and priorities in five broad areas that encompass current activities and provide a framework for considering the future. These are: building and organizing the Library's collection; locating and gaining access to medical and scientific literature; obtaining factual information from databases; Medical Informatics; and assisting health professional education through information technology. The plan is expected to be completed and presented to the NLM Board of Regents for their consideration this year.

One of the most serious deficits faced by health professionals in retrieving information is the lack of a practical unified medical language system that would permit communication between the many and varied health information systems. A study was undertaken by NLM staff in FY 1985 to determine the feasibility of developing a Unified Medical Language System. This study, and the encouragement of outside research groups who were consulted, has resulted in Congress earmarking funds in FY 1986 for NLM to proceed with developing such a system. The Library will work with the American Medical Association, university investigators, and health professional associations to create such a Unified Medical Language System. The project is a long term one that will eventually integrate a great variety of medical information across the multifarious systems and, by facilitating access to this information, improve the level of health care in this country. Essential to any system developed will be the need for a user friendly access module. A new microcomputer interface designed to assist users without online search training has been developed and will be made available in early 1986.

NLM has statutory responsibility to acquire and preserve Library material pertinent to medicine. However, as pointed out in an NLM study completed in FY 1985, the majority of research library materials are printed on high-acid content paper destined to disintegrate if preventive action is not taken immediately. Data gathered show that 8.8% or 113,000 volumes in the NLM modern collection are so brittle that they must be copied to another medium to ensure long-term preservation of the information they contain. The remaining 91.2% of the volumes must be deacidified to prevent rapid deterioration. The staff study included a comprehensive preservation plan which recommends the utilization of existing preservation techniques such as microphotography but also emphasizes investigating other, more modern preservation technologies such as optical disk storage. The preservation plan recommends that NLM take the following actions: (1) establishment of a four-year program for preservation microfilming of deteriorated volumes; (2) expansion of research in the use of mass disk storage for preservation, in coordination with the research efforts of the Library of Congress and the National Bureau of Standards; (3) acquisition of deacidification services for the bulk of the NLM collection that will benefit from this treatment; (4) promotion of the use of acid-free paper for new biomedical publications; and (5) development of a national plan for the preservation of the biomedical literature that encompasses material held by other U.S. organizations. In FY 1986 additional emphasis will be placed on the implementation of this plan with the awarding of a major contract for the microfilming of deteriorated materials.

Acquiring and providing access to the world's biomedical literature is NLM's primary mission. In FY 1985 NLM added some 293,000 items to a collection which now consists of more than three and a half million books, journals, technical reports, theses, pamphlets, manuscripts, microfilm, and pictorial and audiovisual materials. Responding to the changing needs of the biomedical community and the increased usage of microcomputers, NLM acquired for the first time in FY 1985 a limited number of software packages as part of a pilot project.

In FY 1985, the Library cataloged over 17,000 books, journals and audiovisual programs and added indexing for approximately 300,000 journal articles to NLM's computerized database system, MEDLARS.

With the proliferation of microcomputers, which can be used to access NLM's computerized databases, many individual health professionals and researchers wish to search MEDLARS directly rather than through their library or other intermediaries. Such usage of the MEDLARS system has increased dramatically during FY 1985, due in large part to the many special training classes in online searching conducted by librarians throughout the country using materials prepared by NLM. Online services continue their impressive growth. Three million searches were done this year by some 3,400 network member institutions and individuals. In FY 1985, NLM took a number of steps to make its online system more accessible and easier to use. NLM inaugurated around-the-clock service, seven days a week in June, 1985.

The Library's Toxicology Information Program (TIP) is assisting in the critical and scientifically complex, high national priority area of identifying and providing data and information about chemical substances to which humans and the environment are exposed. An important aspect of this activity has been the development and testing of microprocessor-based database management software to facilitate retrieval of information about chemical substances. Such software mounted in movable workstations is capable of supporting emergency response teams at the site of a chemical spill or other hazardous waste emergency. This workstation is now being tested at the Centers for Disease Control, headquarters and several Regional Offices of the Environmental Protection Agency, the National Library of Medicine, and several private organizations. Also, the new online file building, review and search system, TOXNET, containing the Toxicology Data Bank and the new Hazardous Substances Data Bank was opened for public use in July 1985.

NLM has built a constructive relationship with information producers and vendors in the private sector while at the same time protecting its own vital mandate. A policy of collaboration with private sector firms on appropriate information services has been established and agreements to collaborate with commercial firms to create videodisc versions of NLM bibliographic files for test marketing and experimental evaluation have been signed. Through such efforts, new and innovative products and services will be created to assist in the effective dissemination of biomedical information.

The MEDLARS (Medical Literature Analysis and Retrieval System), NLM's computerized database system, produces many bibliographic publications, indices and literature searches. Important examples are Index Medicus, a major index to 2,730 biomedical journals, and specialized literature searches on acquired immunodeficiency syndrome (AIDS). In addition to providing intellectual access to biomedical literature through publications and online databases, NLM also helps health professionals to obtain copies of actual documents. In FY 1985 the Library received 144,000 interlibrary loan requests, and 246,000 requests for materials from the Library's "closed stack" collection (for use by patrons in the Reading Room), and responded to over 91,000 requests for information and reference assistance from outside and remote users. NLM maintains an excellent response rate to these requests in its effort to provide information quickly.

NLM's automated support to locating and requesting documents was improved substantially in FY 1985. For onsite users, an improved version of CITE/CATLINE, NLM's prototype online catalog, became available. For users across the country, the new DOCLINE system, a nationwide interlibrary loan request and referral system was inaugurated. DOCLINE, now coming into widespread use, will greatly speed up the lending process among health science libraries by routing requests automatically through the Regional Medical Library network.

In FY 1985, budgetary increases enhanced NLM extramural programs in Medical Informatics research and stimulated interest among investigators in the field. A major award was made for comprehensive research and training activities in Medical Informatics at a leading medical center. Medical Informatics is a multidisciplinary field, involving the integration of computer and information sciences, medicine, engineering, and management science. The ultimate goal of such research is to develop computerized systems with which human users can consult interactively--

much in the same way that physicians and scientists now consult with their colleagues—to improve medical care and medical decision making and to enhance scientific discovery. The Congress also provided a modest increase in FY 1986 for this program. The IAIMS (Integrated Academic Information Management Systems) program produced several awards to academic medical centers for the development of prototype systems, which can serve as models for other such centers nationwide. The IAIMS initiative is an effort to create model computerized information systems that will serve health professionals in complex academic health centers. From a single desk top terminal, there will be rapid access to various files and systems: patient records, laboratory tests and results, the professional literature through systems such as NLM's MEDLARS, remote files such as a tumor registry in another state, clinical decision-making systems such as those being developed under NLM's Medical Informatics program, student records, and communicating with colleagues. Progress in this important program is continuing in FY 1986.

NLM has created an in-house capability to develop artificial intelligence systems. Library staff have refined the AI/RHEUM diagnostic system in rheumatology as preparation for its validation and evaluation as an example to improve the therapy recommendation system and test it with additional clinical cases. A group of medical professionals from appropriate specialty organizations will work with individual field test sites during the validation process.

Finally, this year, 1986, the National Library of Medicine observes its sesquicentennial, marking a century and a half of service to this nation's biomedical community. To ensure that the Library's services are better known and their contribution to society maximized, a series of sesquicentennial activities has been planned throughout the year. The emphasis is on education and outreach-oriented programs for the health community, including an agenda of scientific symposia.

National Library of Medicine

Extramural Programs

1987 Authorization: $13,000,000 for Medical Library Assistance Act Programs; Indefinite for Medical Informatics programs.

Budget Authority:

1986 Appropriation	1986 Available after sequestering	1986 Revised Estimate	1987	Increase or Decrease
$17,831,000	$17,297,000	$17,297,000	$11,906,000	-$5,391,000
		(FTEs: --)	(--)	(--)

Purpose and Method of Operation

Biomedical communication is essential for the continued advancement of medical education, practice and research. The National Library of Medicine's assistance programs are the unique Federal focal point for a nationally coordinated effort to make the full range of health knowledge available when and where it is needed and in a form which assures its proper interpretation and effective application.

NLM assistance awards make possible a broad range of programs for better management, dissemination, and use of health knowledge. As the results of modern biomedical research show increasing promise in improving patient care, so must the mechanisms for organizing, retrieving, integrating, and using this information be improved.

NLM assistance awards sponsor research investigations and research training in medical informatics and programs to promote the integration of various systems to improve the management and delivery of information, and work in support of the nation's Regional Medical Library Network. NLM's grant and contract programs complement one another in achieving the overall goal of improved health care through the rapid, efficient, and effective communication of knowledge.

Rationale for Budget Request

The FY 1987 budget request for NLM's Extramural Programs is $11,906,000, and will support 96 awards. This represents a decrease of $5,391,000 and 3 awards from the 1986 revised estimate. All commitments made in previous years will be honored. In FY 1987, $1,877,000 would be available to support 32 new investigator-initiated grants, a reduction of $270,000 and 4 awards from FY 1986.

Medical Library Assistance
Title IV, Part D, Sections 469-477, PHS Act

Integrated Academic Information Management System (IAIMS) Program

The IAIMS concept is to use computer and communications technologies to create information systems that integrate operational and academic information in support of health research, education, patient care, and management. NLM currently awards grants to institutions for IAIMS strategic planning and for IAIMS plan testing and model development. Grants are also awarded to support research related to IAIMS activities.

Recent reports by the Association of American Medical Colleges, the Association of Academic Health Centers, and other health professional organizations, have all identified the critical need to improve information management and utilization in the health sciences. Although health care is extremely information intensive, until very recently little attention and fewer resources have been devoted to the systematic capture, storage, management, and delivery of health knowledge in medical centers. The highly efficient library bibliographic networks developed over the past 20 years are not well integrated with internal medical center information systems. These internal systems, furthermore, are proliferating in an uncoordinated fashion. The majority of health center faculties lack sufficient experience to exploit emerging computer and communication technologies for significant improvements in information utilization.

Education in the health sciences is beginning to shift from a memory-based curriculum to a conceptual and problem orientation. In the report Physicians for the Twenty-First Century, a major recommendation is for a reduction in the amount of factual information students are expected to memorize. To do this, medicine must develop and incorporate advanced computerized systems to provide factual information from the literature that can be easily combined with patient and research data. Under the IAIMS Program, NLM will assist health science centers in their shift from outmoded systems and concepts to those that will enable the most sophisticated and effective participation in an increasingly complex electronic environment. Large scale, institution-wide integrated information systems, carefully planned and implemented, will provide the basis for organizing and utilizing health knowledge in new ways to significantly advance patient care, education and research in the medical sciences.

NLM provides grant support to assist in the planning and development of IAIMS, and in the conduct of research related to IAIMS activities. Baylor College of Medicine, University of Cincinnati Medical Center, Harvard Medical School, Johns Hopkins University School of Medicine and the Oregon Health Sciences University are in the planning stages. As a result of successful strategic planning effort and the creation of an institution-wide IAIMS Plan, Columbia University, Georgetown University, the University of Maryland at Baltimore, and the University of Utah are testing IAIMS concepts on a small scale.

Planning and development of IAIMS at medical centers already have identified many unanswered fundamental research questions that go beyond the difficulties of establishing electronic and administrative linking of independent computer systems. Accordingly, in January of 1985 NLM began the IAIMS Research Grant Program and invited investigator-initiated research applications for innovative projects to support the development and implementation of IAIMS. The first three IAIMS Research Grants were awarded in FY 1985 to the Baylor College of Medicine, Georgetown University, and the University of Utah. In FY 1986, funding was continued for planning and concept testing, leading to full-scale implementation of IAIMS by three or four institutions in FY 1987.

IAIMS activities have provided a locus for a multitude of studies, research and developments projects, to improve information access and use in the health science. IAIMS sites are developing as multidisciplinary centers bringing together experts in medical informatics, knowledge organization, clinical decision systems, computer and communication networking, education and training, and health administration and management for unique and highly creative joint effort to address problems of integration of health information.

Medical Library Resource Grants

Resource Grants are intended to assist in the improvement of the nation's health sciences libraries by expanding their resources and services. They are of two types--the Resource Improvement Grant and the Resource Project Grant. Since these grants provide start-up assistance, substantial institutional cost-sharing is required to assure that the resources and services initiated with NLM funds will be continued when that support terminates.

Health science libraries continue to be the first-line constituency of the National Library of Medicine. They are the intermediaries for many of NLM's efforts of service intended to benefit the health care worker, the health educator, and the research investigator. The Resource Grant Program is important not only for the direct improvements it effects in grantee libraries, but for the residual benefits that it provides in maintaining a strong coalition between NLM and more than 5,000 practicing health science librarians.

The Resource Improvement Grant, which is available to single health sciences institutions, as well as consortia of health sciences organizations involved in research, education, and/or patient-care, supports the development of basic literature collections. Consortia promote partnerships of libraries among community colleges, public libraries, hospitals, and health agencies. In recent years, commensurate with the important NLM principle of equal access to health information, Resource Improvement Grant recipients have been primarily located in remote areas, for example, Elko General Hospital in Nevada, Gritman Memorial Hospital in Moscow, Idaho, and Alice Hyde Hospital in Malone, New York. Similarly, library consortia have been developed in Billings, Montana, Eureka, California, and Fargo, North Dakota.

Resource Project Grants are directed towards health sciences libraries to undertake new services and to expand existing ones. Support is available up to three years depending upon the nature of the project. Projects range from the organization and preservation of nationally important historical collections to the use of computer technology to expedite library services. Resource Project Grants are increasingly of the type that make access to library resources more convenient and in a more timely manner. For example, the Health Sciences Library at the University of Maryland received Resource Project Grant support to enable faculty, staff, and students to directly access its reference, online searches, photocopy, and interlibrary loan services from the users' personal computers. For health professionals in rural, underserved areas of Oklahoma, the University of Oklahoma's Health Sciences Center Library staff is offering consultation on searching the literature from office microcomputers. The consultant will develop and deliver instruction and assistance to health professionals wishing to perform their own searches with microcomputers. The consultant will also develop and deliver instruction via an interactive radio-telephone network to those sites where travel is not possible.

Research Grants in Librarianship and Information Science

NLM offers assistance for research and research career development opportunities in Health Science Librarianship/Information Science as well as research relevant to IAIMS and Medical Informatics. Investigations in this program area include studies of managerial and organizational structure for improved information service, studies of how health information professionals perceive their information requirements, and how medical institutions can utilize new technologies for higher levels of information access.

An example is an award to Mt. Sinai School of Medicine to analyze the scientific validity of the literature of controlled clinical trials. The trials, as reported in the literature, are compared to those which are not published. The long-term goal is to develop better criteria for designing controlled trials and for editing the reports of such trials in medical journals.

Publication Grants

This program provides short-term financial assistance to prepare and publish biomedical scientific publications of use to the health professional community. Studies funded are not-for-profit projects and include critical reviews and monographs which identify the present or past status of research and practice in various health fields; publications in the fields of medical librarianship, health information science, and biomedical communications; and translations of significant foreign language monographs and proceedings of scientifically significant conferences related to U.S. priority health needs. This program is one of the very few sources of support for scientific biomedical publications, either within the Federal Government or from private foundations or the commercial sector. Its continuing importance to the health sciences community is attested to by a wealth of favorable opinions appearing in book reviews of grant-supported products.

A study published in 1985, as the result of an earlier award, is a book on *Human Underwater Vision: Physiology and Physics*, which presents current knowledge about vision, visual perception, and the visual system under water. The information summarized comes from international deep sea diving research conducted over a twenty-year period. No similar book exists in any language and the author is the nation's leading expert in this field. A very recent award in this program funds the preparation of a comprehensive, state-of-the art review of research and practice relating to ancillary test ordering practices among American physicians. The final publication is expected to provide much needed information on ancillary service charges, which can represent nearly fifty per cent of the average hospital bill in the United States.

Training

NLM supports postdoctoral research training in the relatively new field of medical informatics. There is a need for qualified, talented investigators, well-equipped to address fundamental issues in the management of health knowledge. The training curricula are multidisciplinary, involving medicine, the cognitive sciences, information science, and computer science. Each training site offers an excellent setting for didactic instruction; involvement in major, ongoing health computer science studies; and opportunities for work in advanced information science research.

In recent years, a community of workers in medical informatics has become established, with professional linkages extending among numerous cognitive disciplines. As the field has grown, investigators have shifted attention from using computers as tools, to gaining better understanding of the cognitive processes and problems. It is now clear that fundamental issues of the structure of knowledge and its role in problem solving, rather than studies of technological application, require probing scientific investigation.

Subsequent to their training period, these newly-trained investigators will contribute to the growth of science by their research and by their leadership in the utilization of information management in clinical decision making in their institutions.

In FY 1987, NLM will continue the support initially provided to five institutions in FY 1984 for research training curricula, and will continue to encourage grant applications for career development in the medical informatics research field.

In addition, in 1987, NLM will establish the framework for the future of this critically important program. Current institutional awards will terminate in FY 1988, and the continuity of NLM's medical informatics training effort should not be interrupted. Planning for its future will begin with a major meeting of training program directors, trainees, and NLM staff in March of 1987.

Medical Informatics
Title I, Part A, Section 301, PHS Act

Medical Informatics Research

The Library's priority research initiative in Medical Informatics continues to assist an emerging discipline of growing importance to the entire health community. This comprehensive program supports research projects of various kinds, career development of promising young investigators, and highly focused research career training at the postdoctoral level. Fiscal year 1985 increases and 1986 sustainable levels of support have contributed toward the identification of this initiative as a viable NLM endeavor.

The expanding scientific dimension and extreme complexity of modern medicine is increasingly directed to patient care through powerful computerized adjuncts to the processing and organization of medical knowledge, information, and data. Appropriate utilization of these powerful devices raises numerous challenging theoretical and practical issues about attributes and utilization of health knowledge. Current research into organization, representation, and utilization of medical knowledge indicates that the future computer role will be immensely larger than it is today. The health care community, particularly in academic medical centers, is increasingly aware of this potential and seeks effective ways of directing it. Methodologies particularly relevant to these issues include artificial intelligence, the cognitive sciences regarding clinical decision making, and linguistic analysis of medical nomenclatures.

NLM's Medical Informatics program is the only program that emphasizes knowledge issues in medicine, and encourages a wide variety of investigators to address them in specific terms. This research applies to the full spectrum of health care, research, and education; its results are frequently of considerable interest also to the general fields of computer and information science. NLM-supported investigators are widely recognized as leaders in this growing field.

The scientific community's response to NLM's recently announced Medical Informatics program goals has been truly gratifying. New work supported includes a major award to the Massachusetts Institute of Technology for research linking medical artificial intelligence with clinical decision making in the medical domains of cardiology and nephrology. Within the project is a series of investigations which articulate fundamental issues of knowledge representation which, while at the theoretical limits of the field, are nonetheless clinically realistic and relevant. At the University of Pittsburgh an expert system is being developed which will take computed tomography images, together with other neurological data, encode the information to provide image representation, and subsequently deliver a justifiable diagnosis. The system's inferencing structures will depend on an innovative "truth maintenance" system.

At Stanford University a therapy planning program is being designed which will handle cases beyond the limits of usual written cancer treatment protocols. This research concerns the representation and use of therapy planning strategies employed by expert clinicians as they monitor and adjust treatment for patients with serious diseases. At Boston University a computerized decision support system is being perfected for hypertension care. The system has innovative linkages to a larger medical information system which operates on a patient database.

Bioethics Information Systems

Modern health care and biomedical research are areas of great interest and achievement, but their success and growth raise many moral, legal, and ethical issues. These value issues--bioethics--are the source of an enormous and disparate literature which represents an accumulated cultural experience that must be made available to a wide variety of information users. In collaboration with the Center for Bioethics at Georgetown University, the National Library of Medicine has sponsored the organization and indexing of this complex documentation for a number of years. This bibliographic material is made available through a printed Bibliography of Bioethics, as well as through an online computer service, BIOETHICSLINE, one of NLM's computerized databases. In FY 1985, these services were augmented by the award of a three-year grant for a national reference center and clearinghouse in bioethics. In this way, a full range of information services and access capabilities will be conveniently available nationwide. In FY 1987, NLM will continue its collaboration and support for these major contributions to the humanities in medicine.

Regional Medical Library (RML) Contracts

The Regional Medical Library (RML) network, coordinated by the National Library of Medicine, comprises seven regional libraries, over 100 resource libraries (usually in academic medical centers), and over 4,000 basic health sciences libraries in hospitals and health-related institutions at the community level. Participating libraries share their resources (collections and personnel expertise) to provide timely access to authoritative biomedical information needed by the nation's health professionals.

While the idea of regional cooperation is often talked about, the practical nation-wide regionally based system of actively cooperating health sciences libraries is a singular achievement. More than 2 million documents are supplied through this multi-tiered RML system each year, the majority (between 70 and 80 percent) are fulfilled within 24-48 hours. Under NLM leadership, the network has set an example for the nation's research libraries. It has done more than organize and support a coherent document delivery network; it has improved access to biomedical information in under-served areas through decentralization of collections and services. In two rural northeast states, for example, in a 4-year period, the ability of hospital libraries to respond to interlibrary loan requests rose from filling 24 percent to filling 76 percent. The RML network has equalized access through efforts to establish national performance standards and service fees. It promoted the diffusion of online technology development and use through extensive consultation and training activities.

The goals of the RML program are: 1) to improve access to and delivery of information to health professionals; 2) to develop and maintain an effective and efficient network of health sciences libraries; and 3) to develop and maintain linkages between the network and other library/information networks or health professional organizations to share resources. The RML network continues to support the use of biomedical research results reported in the medical literature. In order to allow greater program continuity and provide sufficient time for the development of new regional programs, the RML contract period has been changed from three to five years.

National Library of Medicine

Intramural

1987 Authorization: Indefinite

Budget Authority:

1986 Appropriation	1986 Available after sequestering	1986 Revised Estimate	1987	Increase or Decrease
$39,675,000	$37,925,000	$37,925,000 (FTEs: 413)	$38,895,000 (413)	+$970,000 (--)

Purpose and Method of Operation

Unlike most other components of the National Institutes of Health, the activities of the National Library of Medicine do not fall neatly into the categories of "intramural" and "extramural." In addition to in-house research and development, all of the NLM programs described under the intramural rubric provide information services or products to other health-related institutions--Federal, academic, and industrial. NLM's intramural activities are carried out by three major components:

- Library Operations--selects, acquires, preserves, catalogs, indexes, provides access to, and disseminates the material in NLM's collections;
- Lister Hill National Center for Biomedical Communications--performs research and development to create new, or modify existing biomedical communication systems and networks; designs, tests, and evaluates modern educational methods and audiovisual technologies.
- Toxicology Information Program--develops specialized information services in the fields of toxicology, pharmacology, and the environmental sciences.

Rationale for the Budget Request

The FY 1987 budget request for Intramural programs is $38,895,000 and represents an increase of $970,000 above the FY 1986 revised estimate. This increase will offset a portion of mandatory cost increases. The NLM will continue to provide basic library services to the biomedical community, and will continue support for its preservation program and Unified Medical Language System initiative.

Library Operations

Library Operations is the component responsible for NLM's basic mission--to build, maintain, and provide access to the world's largest collection of biomedical literature in support of the progress of medicine and the improvement of public health. No other organization, public or private, duplicates NLM's comprehensive biomedical information activities. Library Operations primary tasks are: (1) acquisition of the biomedical literature; (2) preservation of that literature; (3) creation of bibliographic data; (4) dissemination of the data in a variety of formats; (5) document delivery and reference service; and (6) support of scholarship in the history of medicine. NLM is committed to evaluating and using new technologies to improve its ability to provide these important services. The Library also promotes cooperation among the national libraries to enhance the effectiveness and efficiency of library service in the United States.

Beginning in FY 1986, NLM program and contract administration staff are procuring a data communications service package on behalf of the Department. NLM experience with large communications contracts combined with high volume of usage should result in an efficient and cost-effective procurement of these services for DHHS.

Acquisition

One essential function of Library Operations is to identify and acquire rapidly new and retrospective library materials, ensuring that the collec- tion continues to meet the needs of the nation's health professionals. The Library collects materials comprehensively in some 40 biomedical areas and, to a lesser degree, in related subjects such as general chemistry, physics, zoology, and botany. Presently, the collection consists of more than three and a half million books, journals, technical reports, theses, pamphlets, manuscripts, microfilm, and pictorial and audiovisual materials. The Library's collection provides the basis for its major service programs and serves as backup for health sciences libraries throughout the country. In FY 1985 NLM acquired approximately 27,000 books and audiovisual programs, 125,000 serial issues representing 23,000 individual titles, and 193,101 modern manuscript items. For the first time, NLM acquired a limited number of software packages on biomedical subjects, as part of a pilot project to determine the resources needed to acquire and catalog these items.

In May 1985, NLM published a new *Collection Development Manual of the National Library of Medicine*, which guides staff in the selection of items for the collection. The new manual supersedes the 1977 edition and is the product of a two-year effort to revise NLM's selection criteria to reflect the changing needs of the U. S. biomedical community. In order to clarify the collecting responsibilities of the three national libraries, NLM's new manual incorporates information about the collection development practices of the Library of Congress and the National Agricultural Library (NAL) in fields related to medicine. NLM and NAL also published a joint statement explaining the collection development policies of the two national libraries in the field of veterinary science. In order to determine whether NLM's collection development guidelines and their interpretation by staff result in a collection that meets the needs of health professionals, the Library evaluates the content of the collection and of the NLM indexing service in one or two selected subject areas each year. In 1985, staff looked at NLM's coverage of the field of medical informatics. In 1986, health services research and some aspects of veterinary medicine will be examined.

Preservation

Ensuring the present and future availability of the biomedical literature is another critical Library responsibility. In FY 1985, NLM staff completed the development of a comprehensive preservation plan which will guide the Library's preservation efforts for the next five years. A survey of the physical condition of the NLM modern collection conducted as part of the planning effort revealed that 8.8%, or 113,000 volumes, in the NLM collection are so brittle that they must be copied to another medium if the information they contain is to be preserved. The remaining 91.2% of the volumes must be deacidified to prevent rapid deterioration. NLM's preservation plan recommends several actions including: (1) creation of a Preservation Section; (2) establishment of a four-year program for preservation microfilming of deteriorated volumes; (3) expansion of research in the use of electronic storage for preservation, in coordination with the research efforts of the Library of Congress and the National Bureau of Standards; (4) acquisition of deacidification services for the bulk of the NLM collection that will benefit from this treatment; (5) promotion of the use of acid-free paper for new biomedical publications; and (6) development of a national plan for preservation of the biomedical literature that encompasses material held by other U. S. organizations. Work is proceeding to establish the Preservation Section, which will implement several of these recommendations. The Lister Hill Center will pursue its research on the preservation uses of optical disk technology. During 1986 NLM will support the initiation of a major contract for preservation microfilming of deteriorated materials and special preservation of items in the historical collections.

Creation of Bibliographic Data

The NLM is charged with the responsibility for organizing the biomedical literature it acquires by appropriate cataloging, indexing, and bibliographical listing, and making this bibliographic information available through publications and other appropriate means. Without these efforts, the literature NLM acquires would be inaccessible and therefore seriously limited in its usefulness. By performing these functions, NLM not only provides access to its own collection, but also reduces the amount of staff required for cataloging and indexing in other U.S. biomedical libraries. This saves the total U.S. biomedical library community several million dollars annually.

A basic part of NLM's service mission is to create authoritative cataloging and indexing records. In FY 1985, Library Operations cataloged about 17,200 books, journals and audiovisual programs and added indexing for more than 299,000 journal articles to NLM's computerized database system, MEDLARS (Medical Literature Analysis and

Retrieval System). Online record creation systems assist catalogers and indexers to create high-quality records through automatic validation and error checking features and also help to reduce the time required to make completed records available to NLM's users. In FY 1985, local contract indexers also began to use the online indexing system. The Library continually investigates methods to make its cataloging and indexing operations more effective and efficient. NLM is cooperating with the Library of Congress and the National Agricultural Library to explore the application of artificial intelligence techniques to the development of an expert cataloger system; NLM staff are also investigating ways to use machine-readable journal data to speed the indexing process.

NLM and the Library of Congress (LC) share cataloging expertise in several ways. NLM receives assistance from LC in cataloging materials in certain languages for which NLM staff do not have the necessary expertise. LC uses descriptive cataloging prepared by NLM for clinical medical books produced by U.S. publishers who participate in the Cataloging in Publication program. NLM and LC have access to each other's automated cataloging files, and NLM is a regular contributor to LC's National Authority Cooperation Project. NLM is also engaged in developing a machine-readable mapping of its Medical Subject Headings (MeSH) to equivalent terms in the Library of Congress subject heading system. When completed in two to four years, the map can be used to improve retrieval of medical literature in the many large online catalog files that contain some records indexed with terms from the NLM Thesaurus and some with the LC Thesaurus.

Dissemination of Bibliographic Data

The bibliographic data in the MEDLARS system is distributed in three ways: in a series of printed publications, in machine-readable formats, and online. NLM produces many bibliographic publications, ranging from Index Medicus, NLM's major index to 2,730 biomedical journals, to a quarterly published literature search on acquired immunodeficiency syndrome (AIDS). An important publication initiated in 1985 is the microfiche NLM Catalog, which includes information about virtually all cataloged titles in the NLM collection. The base catalog contains records for 575,000 works published from 1480 through 1984 and cumulates records from a number of older NLM catalogs. It will be kept up to date by a quarterly cumulative supplement covering works from 1985 on.

There are 27 MEDLARS databases and datafiles available for distribution in machine-readable formats. Of these MEDLINE is the largest and most frequently distributed. NLM's databases are leased by commercial database vendors, non-profit U. S. institutions, and foreign institutions, most of which in turn offer online access to MEDLARS data. In FY 1985, NLM dispatched 2,000 tapes of various databases to 31 domestic and foreign licensees. In order to make its cataloging records easily usable by the library community, NLM distributes them in standard MARC (Machine Readable Cataloging) format. In FY 1985, NLM's audiovisual cataloging records became available in this format for the first time. All NLM cataloging records are now available in MARC. The Library also began to distribute subsets of the MEDLINE database to U.S. individuals and institutions this year; there were eight subscribers to this service at year's end. NLM has entered into agreements with several commercial firms to allow them to produce laser disk copies of MEDLINE data on an experimental basis.

As the number of organizations providing access to MEDLARS data increases and the ways in which the data are made available proliferate, quality control of the data becomes increasingly difficult. NLM has an inherent responsibility to maintain the quality and integrity of its databases since the distribution of accurate and complete data is essential to fulfill the Library's statutory responsibility "...to assist in the dissemination and exchange of scientific and other information important to the progress of medicine and the public health... ." To a great extent, NLM staff can control the quality of the data on the NLM system and ensure that records are accurately stored and updated and that they may be accessed through an adequate retrieval system. The Library must devise acceptable methods to exert control over how licensees of MEDLARS data store, update, and provide access to NLM records and how they represent the source, content, and uses of these records. If licensees fail to provide complete, up-to-date MEDLARS data through a reliable retrieval mechanism, the user may not retrieve accurate, up-to-date data and the NLM staff effort to maintain the quality of the databases is negated. Public confidence in NLM as a source of accurate, up-to-date information may also be diminished. NLM has recently modified the tape license agreement to include requirements for maintenance and correction of the files and is developing methods for testing the quality of MEDLARS records available on and retrieved via other systems. After the quality control issue is resolved, the Library will implement a new policy to permit domestic licensees to redistribute portions of the MEDLINE file.

NLM also provides direct online access to its databases. As of the end of FY 1985, 3,621 domestic institutions and 630 individuals had online codes to access the 27 MEDLARS databases on the NLM computer system. The number of individual health professionals and researchers using the system increased 326% during FY 1985, due in large part to the many special training classes in online searching for health professionals conducted by librarians throughout the country using materials prepared by NLM. The total annual usage of NLM's MEDLARS system was 235,360 connect hours.

In FY 1985, NLM took a number of steps to make its online system more accessible and easier to use. Hours of availability for the online system were extended to around-the-clock service, seven days a week. The monthly minimum charge for each online access code was discontinued; users are now charged only for actual system usage. The new user-friendly TOXNET system, which provides access to chemical, toxicological, and hazardous waste data became available to all users of NLM's MEDLARS system. A new microcomputer interface to MEDLINE, designed to assist users without online search training, has been developed and will be made available in early 1986.

A major program to modernize NLM's computer services is the development of MEDLARS III. MEDLARS III will be a new generation of the Medical Literature Analysis and Retrieval System, NLM's pioneering computerized system for handling the biomedical literature. MEDLARS III is intended to improve, extend, and integrate such internal library operations as ordering, receiving, cataloging, and indexing materials. It will also enhance the external network capabilities which allow NLM to build and maintain its online retrieval files and to provide support services to the Regional Medical Library Network. When complete, the full system will reduce duplicate effort in creating and maintaining bibliographic data; provide enhanced computer assistance to receipt processing, cataloging, and indexing; permit automated inventory control of each physical item in the NLM collection; eliminate artificial segmentation of bibliographic records into multiple files that complicate online searching for NLM's users; and provide a more easily used retrieval system. The first phase of the system, which includes the database management software as well as an integrated system for monograph acquisitions and cataloging, is being developed under contract by Logicon, Inc., and is scheduled for delivery in 1986.

NLM has completed the design and installation of a Local Area Network and installed nearly 200 connections; this will link the MEDLARS III workstations to NLM's central computer operating system.

Document Delivery and Reference

Another method of disseminating biomedical information is through lending or copying portions of materials from the NLM collection and providing reference and research assistance to health professionals. In performing these functions, NLM provides an effective back-up service for the nation's biomedical libraries and equalizes access to biomedical information for users in different geographic areas with varying local biomedical information resources. In FY 1985 Library Operations received 144,000 interlibrary loan (ILL) requests and 246,000 requests for materials from the Library's "closed stack" collection (for use by patrons in the Reading Room). Excellent fulfillment and throughput rates were maintained for book and audiovisual loans, photocopies, and Reading Room requests. In FY 1985, NLM's loan service was expanded to cover all audiovisual programs in the NLM collection.

There are four general steps in the process of document delivery: identifying the document needed, locating it, requesting it, and transmitting the document to the requestor. Through its publications and online databases NLM announces the availability of materials so that users can identify needed items. NLM's automated support to locating and requesting documents was improved substantially in FY 1985. For onsite users, an improved version of CITE/CATLINE, NLM's prototype online catalog, became available to onsite users. For users across the country, the new DOCLINE system, NLM's automated document request and routing system, became available for use by health sciences libraries in NLM's Regional Medical Library Network. One hundred thirteen network libraries were using the system at the end of FY 1985; this number should grow to 1,000 by the end of 1986. DOCLINE is linked to MEDLINE, CATLINE, and AVLINE to facilitate generating requests. It uses data in SERHOLD, NLM's computerized serials holdings database, to identify which libraries own requested journal articles and to route requests to those libraries automatically. SERHOLD now contains more than 815,000 holdings statements for some 1,850 U. S. biomedical libraries. Other efforts to enhance automated support to requesting documents included expansion of the number of electronic mail systems from which NLM accepts document requests and a test project to receive automated document requests from OCLC (Online Computer Library Center).

DOCLINE does not address the fourth step in the document delivery process, that of transmitting the document to the requestor. Telefacsimile technology is one option for reducing the amount of time required to transmit the document itself. In FY 1985, NLM used telefacsimile equipment to fill three emergency requests from hospitals to provide articles related to critical patient care problems. NLM intends to test broader use of telefacsimile for document delivery in FY 1986.

In FY 1985, NLM responded to almost 91,000 requests for information and reference assistance from onsite and remote users. NLM staff members provide special information service support to the NIH consensus development conferences and respond rapidly to a variety of special information requests from members of Congress, the Supreme Court, the Office of the President, The Secretary of the Department of Health and Human Services, and other federal agencies.

Special Historical Programs

NLM has unique and extensive collections of rare books, manuscripts, pictures, theses, and historical pamphlets which are a valuable resource to scholars throughout the world. The Library sponsors a number of special activities to promote continued growth and increased use of these rich collections. In FY 1985, NLM initiated a new Visiting Scholar Program, which invites a recognized historical scholar to spend six to twelve months at the Library. Participating scholars are expected to engage in research that will use the NLM historical collections extensively. They also provide consultation to NLM staff, make one or more public presentations, and assess segments of the NLM collection. Dr. Thomas Hall participated in the prototype of the Visiting Scholar Program in 1985. Dr. James Harvey Young, the first competitively selected Visiting Scholar, will come to the Library in 1986. In addition to this program, NLM has also contracted with Dr. Morris Collen to write a history of medical computing using materials available at NLM and elsewhere and to advise the Library on important documents in this field. Throughout NLM's sesquicentennial year, NLM's historical resources will be highlighted in a variety of exhibits and presentations.

Lister Hill National Center for Biomedical Communications

The research programs of the Center focus on the information needs of the biomedical community and matching those needs with the potential solutions in evolving communications and information technologies. The Center continues to pursue programs which exploit the computer and to understand its potential for interaction with health professionals. Research at the Center includes areas such as: expert systems, automated classification and retrieval, electronic preservation, and videodisc-based computer assisted instruction.

Creation of a Unified Medical Language System

A ten year program is being planned by the NLM to take the lead among interested American health care constituencies in planning and executing steps that would result in a computer based system of uniform and coordinated medical language vocabulary, including terms for access to the medical scientific literature and terms for recording and coding patient records. Working with the American Medical Association, university investigators in academic departments, and health professional educators, NLM will initiate and coordinate a program to create a Unified Medical Language. The program will be guided by an advisory committee whose members represent these groups and also the insurance industry and relevant governmental agencies.

The system will include such items as a dictionary, thesaurus, cross-indices between selected codifications, automated classification and indexing assistance tools, and computer programs to link literature and medical records. While a complete system is a long term undertaking, useful intermediate products should rapidly become available that will increase efficiency of current operations and contribute to better data collection regarding health care. These results potentially could lead to significant savings in direct care delivery.

It should be emphasized that this Program initiative is at least as large an undertaking as the creation of the original MEDLARS system itself, and intellectually a great deal more difficult. Because of NLM's internal competence and its politically neutral position, there seems a good possibility NLM could succeed in gaining cooperation from the diffuse elements of the American health care professions and information industries—at least for this important undertaking. It is likely that no other institution could do this; to date, none has attempted to do so. Accomplishing this program will be relatively expensive in NLM terms, but trivially inexpensive in terms of current health care expenditures such as the HCFA reimbursements.

During FY 1985, NLM began planning for the Medical Language Project. Initial exploratory work has begun to assess the boundaries of the problem and to characterize the relationships between the vocabulary of the biomedical research literature and that of the clinical setting.

Artificial Intelligence/Expert Systems Project

Computer scientists have recently discovered how to build computer programs that provide a good functional equivalent to human understanding and decision making, if the subject area is reasonably narrow. Following this new capability, the medical informatics field has discovered forms of knowledge representation that are suitable for medicine. The result is the emerging capability to build systems that can give reliable and practical expert consultation concerning patient diagnosis and management. The Expert Systems Program addresses research issues in the application of artificial intelligence techniques to the development of knowledge-based consultant systems in medicine and medical education.

In FY 1985 efforts were directed to both the intramural aspects of building an in-house artificial intelligence systems development capability and the extramural aspects of technology transfer, research community-building, and information dissemination appropriate to the mission of the National Library of Medicine.

The NLM now has in-house two functioning medical expert systems. The AI/RHEUM system for consultation in rheumatology has a management component ready for extension from rheumatoid arthritis to additional diseases. The initiation of a multi-site validation study of the diagnostic component is anticipated for AI/RHEUM during FY 986. A central coordinating group will be established, field sites chosen, and equipment purchased for support of field trials. In FY 1987, information and feedback from the trial sites will be used to help perfect AI/RHEUM as a diagnostic consultant system and to extend its utility in the clinical practice setting. AI/COAG, a second expert system at NLM, deals with problems of human hemostasis. It also will warrant field testing in the near future.

Electronic Document Storage and Retrieval Project

The LHNCBC's interest in various electronic and optical technologies arises to a great extent from their applicability in meeting the mission of the NLM. These include the preservation and archival storage of biomedical literature, and the processing of information for use by the medical research and practicing communities. The long term goal of the program is to introduce appropriate advanced technology to help ensure that the Library fulfills its mission as a national archive for biomedical literature. Studies have been done on current preservation activities, present status of preservation techniques and possible strategies to adopt. While possible preservation techniques include microfilming, mass deacidification and strengthening of embrittled paper, digital electronic storage of the images on optical discs is a technique with several advantages. Among these are the ability to store a wide range of material, the ability to process the electronic images to improve their quality over that of the original documents, and quite importantly, the ability to be randomly accessed and automatically retrieved by using existing citation databases as directories.

Questions that remain to be answered with respect to electronic imaging as a document preservation technique include those concerning the cost of the process of preservation, the rate at which conversion may be accomplished, image quality considerations, media longevity and regenerability of the data to ensure information longevity, the strategies and costs associated with quality control, the human-machine interface for higher throughput, and lower error rates, among others. In addition, the availability of experienced researchers and the established laboratory facilities offer an opportunity to investigate the role of electronic imaging in successfully solving the document retrieval problem.

Automated Classification and Retrieval Project

This program encourages research in the development of computer systems to improve and automate the classification of published literature to aid the retrieval of useful information. The areas to be explored include classification, indexing, storage, and retrieval of this information from the biomedical literature.

The Center will examine those methodologies which offer the greatest opportunity for electronically organizing machine-readable data bases to increase the productivity of the indexing and cataloging activities.

Two research projects have been initiated. The first is on knowledge refinement with the objective of identifying methods to incrementally refine and merge hierarchical structures such as MeSH and SNOMED (Systematized Nomenclature of Medicine). The second project, indexors aid, involves the design and development of a system for classifying concepts and relationships in medical articles as frame representations and providing knowledge-based assistance in the assignment of MeSH indexing terms.

Videodisc-Based Computer Assisted Instruction (CAI)

Although computers have now been used for instructional purposes for almost two decades, their use in the medical sciences has been restricted. Recent advances in optical videodisc technology make it possible to use computers and optical discs for education in the health professions. There is renewed interest and enthusiasm among medical educators in sophisticated and creative applications of computer based instruction. The availability of optical videodisc technology and high-resolution television now permits storage and dissemination of high quality medical images, including radiographs and other primary clinical information. New technologies are being exploited to create a series of computer based simulations of the clinical encounter, which will demonstrate innovative and effective use of the new technology in medical education (e.g., admissions, basic sciences, clinical sciences, and practice). The capabilities of the new technology for random access of high quality video and multiple audio tracks coupled with the intelligence capacity of the computer to make possible creation of effective contextual learning strategies. These approaches are being presented to the medical education community at the demonstration center under development at the LHNCBC and at appropriate medical professional meetings.

Online Reference Works Program

The NLM is investigating the opportunities of Online Reference Works (ORW) in medicine. The ORW program investigates the total advantages to be accrued by bringing important existing reference works into an online environment. The goal of the program is to find techniques that produce an enhanced environment for online reference works that encompasses the authoring and editing cycles and improves total accessibility both by improving retrieval and by adding multiple new access points including auxiliary data bases. In collaboration with the Welsh Library at the Johns Hopkins School of Medicine, research is proceeding in the areas of creation and use of software to facilitate editing and revision control, and enhance an author's ability to keep reference works current. As part of the overall effort, the Information Retrieval Experiment (IRX) project will be used as the research tool for retrieval from and access to the reference book. Using the book Mendelian Inheritance in Man (MIM) by Dr. Victor A. McKusick at the Johns Hopkins University as the initial reference work, the IRX is bringing MIM into an online environment. The goal of the project is to first investigate the upper bounds of traditional statistical keyword retrieval, and then begin to modify the tools to allow content identifiers other than keywords, and extensive intelligent interaction with online users. Current research is being done both in a batch-oriented test collection mode, and in an interactive mode with actual users.

While potential gains in terms of a single reference work appear great, and the problems challenging, the integration of multiple reference works in a given area of the health sciences with other complementary information (numeric data, graphics, etc., and ultimately a visual data base) promises even greater returns. Effective access to and organization of information including text, graphics, annotations, etc., is a continuing critical need in all areas and particularly in the health sciences. The rate of change of information in any specialty area, and the need to relate many different facets of information is especially critical. As more reference works become maintained online, there will be a greater urgency to obtain meaningful access to the most current information. By concentrating on individual specialty areas such as genetics, it is feasible to begin modeling and exploring the most effective use of these future environments.

Toxicology Information Program

The Toxicology Information Program (TIP) was established at the National Library of Medicine (NLM) in 1967 in response to recommendations made in the 1966 report, "Handling of Toxicological Information" by the President's Science Advisory Committee. The primary objectives of the TIP are: (1) to create computerized toxicology databases from the scientific literature and from the files of collaborating industries, academic institutions, and Government agencies; and (2) to provide toxicology information products and services to the scientific community. The services of TIP are made available via online information retrieval files and through query response. TIP also works through several interagency agreements which result in providing information products and services to other agencies and to the biomedical community.

Online Services

One of TIP's major functions is the creation and maintenance of online toxicology information services that are part of NLM's MEDLARS system. This began in 1972 when the TIP implemented TOXLINE, the first publicly accessible online retrieval service covering the toxicological literature. This was followed in the same year by the development of CHEMLINE, an online dictionary file that facilitates searching for chemical information in TOXLINE and other NLM information sources.

In 1982, TIP began to provide information support to the private and public sector communities concerned with effectively resolving problems associated with accidental spills of chemical substances and with the appropriate handling of industrial wastes, especially those generated by the chemical industry. TIP support to this massive effort, resulted in large part from passage of the Comprehensive Environmental Response, Compensation, and Liability Act of 1980 (CERCLA or the "Superfund Act"). NLM has been assigned responsibilities for providing data and information to support the requirements of this Act.

A readily available authoritative source of health and environmental information was needed. NLM's online Toxicology Data Bank (TDB) was deemed to be the foundation for the development of an enhanced information resource capable of handling the broader array of data and information required in the area. The resulting new data resource has been named the Hazardous Substances Data Bank (HSDB). The categories of information available in HSDB cover among others the following areas: substance identification, manufacturing/use, chemical/physical properties, safety and handling, toxicology/biomedical effects, pharmacology, environmental fate/exposure potential, exposure standards and regulations, and monitoring and analysis methods.

TIP has greatly improved the online building, maintenance, review and searching of the TDB and HSDB by developing a major new system named TOXNET (Toxicological Data Network) (see under Collaborative Services for more detail). TOXNET now contains two data banks, an expanded version of the TDB and the broader, more comprehensive, HSDB.

TDB and HSDB are online data or fact retrieval services focusing on toxicological information while maintaining a high degree of quality control through review by a committee of experts. In order to respond to the expanded scope requirements brought about by CERCLA, it was also necessary to enlarge the mechanism through which TDB and HSDB content are scientifically reviewed. Accordingly, the ten-year old TDB Peer Review Committee was replaced by a new, 16-member Scientific Review Panel that includes toxicologists, environmental scientists and industrial hygienists. The costs for this review apparatus are shared by NLM and the Defense Logistics Agency, which also uses this panel to review content of records prepared for its Hazardous Material Technical Center (HMTC). NLM, in turn, uses HMTC material for input to the HSDB and to TOXLINE. In FY 1985, TDB and HSDB each contained over 4,100 compound records.

The TDB and HSDB serve the informational needs of the National Toxicology Program, the FDA and EPA, as well as those of investigators in the areas of environmental and health effects of hazardous substances, and the emergency response needs of those responsible for the cleanup and disposal of hazardous wastes and chemical spills. Thus, these files are primary sources of information used by the Center for Environmental Health and the Agency for Toxic Substances and Disease Registry (ATSDR) at the Centers for Disease Control (CDC) in responding to emergencies involving hazardous chemicals. CDC also relies on TDB and HSDB in "emergency simulations" for training personnel responsible for chemical emergency response.

The TIP continuously evaluates and enhances the NLM chemical and toxicological files to optimize their information support functions. During FY 1985, the online chemical dictionary file, CHEMLINE, was subjected to a questionnaire-based survey of users of online chemical databases to determine areas that might be improved to assist the users. As a part of this activity, a major augmentation to CHEMLINE's nomenclature coverage was made through the addition of over 14,000 drug names taken from the "USAN and the USP Dictionary of Drug Names." Other authoritative sources of chemical nomenclature are being worked on for future incorporation. CHEMLINE presently contains approximately 646,000 records for substances covered in other NLM online files, such as TOXLINE and MEDLINE and in EPA's TSCA Inventory of Chemical Substances.

In addition to enriching TOXLINE, NLM's bibliographic file for the toxicological literature, with bibliographic citations related to industrial safety and health as well as information on the transport and disposal of hazardous wastes, TIP has initiated plans to evaluate TOXLINE's subject coverage. This action was deemed necessary to assure that TOXLINE was adequately covering the changing field of toxicology and related sciences and, especially, the burgeoning field of biotechnology and its products. TOXLINE and its backfiles presently contain over 1.7 million references.

RTECS (Registry of Toxic Effects of Chemical Substances) is another NLM online data retrieval file containing acute and some chronic toxicity data for over 78,000 substances. File content is provided to NLM by the National Institute for Occupational Safety and Health (NIOSH). In addition, this file contains information on the status of compounds under various Federal programs and regulations. This year, the TIP enriched RTECS by the addition of Chemical Abstracts Services (CAS) Registry Numbers to records that did not have them. These unique identifiers are critical in linking the RTECS data to other NLM chemical and toxicological files.

DIRLINE (Directory of Information Resources Online), an online directory which refers MEDLARS users to organizations and other sources that can provide information in specific subject areas, has been available as one of NLM's online services since August, 1984. At present, DIRLINE receives records from the Library of Congress' National Referral Center (NRC) database (14,000 records) and from the DHHS' National Health Information Clearinghouse (NHIC) database 980 records). New file segments derived from a Food and Drug Administration (FDA) list of poison control centers, an Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA) directory, and several Health Resources and Services Administration (HRSA) databases are being processed for addition to DIRLINE in FY 1986.

Query Response

TIP's query response and literature search services are provided primarily through the Toxicology Information Response Center (TIRC), a collaborative venture between NLM and the Department of Energy's Oak Ridge National Laboratory. The Center responds, on a fee-for-service basis, to requests for information about the effects of chemical substances on humans, animals, and other compartments of the environment. During the past 12 years, the Center has gained a wide reputation and acceptance as being capable of providing pertinent information, concisely assembled and quickly delivered to such users as physicians, lawyers, researchers, and regulators in both the private and public sectors.

Collaborative Services

TIP collaborates actively with other Government organizations on toxicological information activities. Several joint projects are currently under way through interagency agreements.

As mentioned, a major program to support the DHHS in meeting its responsibilities under the "Superfund Act," was initiated in 1982 and greatly expanded in 1983 through 1985. NLM is responsible for establishing and maintaining "an inventory of literature, research and studies on the health effects of toxic substances," as mandated by the Act. Superfund support to TIP has been very uneven since its beginning in 1982. Variable--and now reduced--funding, and the failure to receive additional personnel slots have weakened TIP's efforts to establish and deliver the "inventory" as quickly and completely as desired. Under these conditions, it continues to be difficult for TIP to plan and maintain a properly structured array of project activities required to support its obligations under the Act.

TOXNET

Utilizing NLM and Superfund resources, the approach--accepted by DHHS and EPA--for developing this "inventory" has been to expand, where possible, existing NLM online databases, such as TOXLINE, CHEMLINE, and the Toxicology Data Bank (TDB), with information relevant to chemicals likely to occur in waste dumps or be involved in chemical accidents. A new computer system, called the Toxicology Data Network (TOXNET) was implemented by TIP during FY 1985 for some of these activities and opened for the public in July 1985. TOXNET is an "umbrella" system of several toxicologically-oriented databanks operated by NLM in parallel with the Library's ELHILL system. TOXNET now contains the expanded version of the TDB file, and the more comprehensive Hazardous Substances Data Bank (HSDB) file. Other related files, such as the National Cancer Institute's (NCI) Chemical Carcinogenesis Research Information System (CCRIS), are being added to TOXNET early in FY 1986.

Microcomputer Workstation

Work continues on developing the microcomputer workstation that is to be used for retrieving and manipulating data and information needed in responding to emergencies involving hazardous chemicals. The workstation uses a microcomputer (or "personal computer") version of the Chemical Substances Information Network software called micro-CSIN. This software had been developed by NLM in conjunction with the Council on Environmental Quality (CEQ) and the Environmental Protection Agency (EPA). Micro-CSIN is designed to translate an online user's request for factual or bibliographic information into the proper format for searching multiple databases, possibly located in different computers, and carry out most of the searching automatically. In FY 1985, this system was field-tested by NLM and ATSDR/CDC on IBM PC XT and AT computers. Further testing by some twenty organizations in industry and Government agencies is also under way. The software will be made available in FY 1986 through the National Technical Information Service.

NLM and ATSDR/CDC also plan to enhance the workstation further for emergency response use, by including relevant subsets of the HSDB file with a chemical directory. This will allow response staff to search either the resident subsets or to retrieve additional information from outside the workstation by accessing remote online databases. Workstations of this type should facilitate access to various important sources of data and information for workers on site at chemical waste dumps or emergency response teams at chemical accident sites.

State/Federal Workshop

A State/Federal Workshop on the Joint Development of Toxicological and Environmental Information Resources, sponsored by the National Governors Association (NGA), Association of State and Territorial Health Officials, EPA, CDC and TIP/NLM was held on May 28-29, 1985, at NLM. The results of this meeting clearly demonstrated that the Federal and State organization responding to hazardous chemical emergencies and concerned with regulating the production, use, transport and disposal of chemical substances, believe that considerable human and fiscal resources might be saved if more relevant information resources could be developed and maintained through joint ventures. TIP/NLM, in conjunction with NGA, and an interagency Workshop Steering Committee is considering what the administrative structure and location should be for an organization to support such joint venture programs. The report from the Workshop will be available early in 1986.

Workshop on Information Activities In Biotechnology

In the Spring of 1986, TIP/NLM will sponsor at the National Academy of Sciences, a workshop to review the status of data and information activities supporting R & D areas in biotechnology. Represented at this Workshop will be users, operators, and supporters of such information activities. It is hoped that the report from this Workshop will identify areas where new activities by NLM and others can facilitate the information transfer, storage and retrieval processes in biotechnology.

TOX-TIPS

TIP produces the publication, TOX-TIPS (Toxicology Testing in Progress) for the DHHS Committee to Coordinate Environmental Health and Related Programs. This monthly current awareness bulletin on Government, industry, and university toxicology testing projects alerts the user community to ongoing research, thereby helping to avoid duplicate testing of chemical substances.

Another aspect of TOX-TIPS is related to the issue of "alternatives to animal testing." The scientific community is concerned with effective animal care and is sensitive to public concerns regarding how and why animals are used in biomedical research and toxicity testing. In FY 1985, TOX-TIPS added an alerting service on recent literature about "animal testing alternatives."

National Library of Medicine

Research Management and Support

1987 Authorization: Indefinite

Budget Authority:

1986 Appropriation	1986 Available after sequestering	1986 Revised Estimate	1987	Increase or Decrease
$5,707,000	$5,456,000	$5,456,000 (FTEs: 91)	$5,607,000 (91)	+$151,000 (—)

Purpose and Method of Operation

Research Management and Support funds the salaries and expenses of the staff who provide for overall administration and direction of National Library of Medicine programs, including the extramural grant and contract programs. Among the functions carried out in this activity are execution of basic administrative services; contracts processing and management; grants management and the scientific direction of NLM's extramural programs, financial and personnel management; coordination of equal employment opportunity activities; direction of NLM's international programs; public inquiries and management of the Library's publications; and operations research. NLM's planning and evaluation activities are also provided for in this activity.

Rationale for Budget Request

The FY 1987 budget request for Research Management and Support is $5,607,000 and represents an increase of $151,000 above the FY 1986 revised estimate. This increase will offset a portion of mandatory cost increases. Through this activity, NLM will continue to provide efficient and effective administrative support and direction for its programs.

National Library of Medicine

Detail of Permanent Positions

	1985 Actual	1986 Estimate	1987 Estimate
ES-4.................	9	9	9
ES-1.................	1	1	1
Subtotal...........	10	10	10
GS/GM-15............	24	24	24
GS/GM-14............	38	38	38
GS/GM-13............	63	63	63
GS-12................	83	83	83
GS-11................	56	56	56
GS-10................	3	3	3
GS- 9................	35	35	35
GS- 8................	19	19	19
GS- 7................	60	60	60
GS- 6................	38	38	38
GS- 5................	40	40	40
GS- 4................	17	17	17
GS- 3................	3	3	3
GS- 2................	1	1	1
Subtotal...........	480	480	480
Grades established by act of July 1, 1984 (42 U.S.C. 207):			
CO-6................	2	2	2
CO-5................	1	1	1
Subtotal...........	3	3	3
Ungraded.............	2	2	2
Total permanent positions.........	495	495	495

TUESDAY, MARCH 18, 1986.

OFFICE OF THE DIRECTOR

BUILDINGS AND FACILITIES

WITNESSES

EDWARD E. NICHOLAS, JR., ACTING ASSOCIATE DIRECTOR FOR ADMINISTRATION, OFFICE OF THE DIRECTOR, NATIONAL INSTITUTES OF HEALTH, DEPARTMENT OF HEALTH AND HUMAN SERVICES

DR. JAMES B. WYNGAARDEN, DIRECTOR, NATIONAL INSTITUTES OF HEALTH

DR. WILLIAM F. RAUB, DEPUTY DIRECTOR FOR EXTRAMURAL RESEARCH AND TRAINING, NATIONAL INSTITUTES OF HEALTH

DR. EDWIN D. BECKER, ASSOCIATE DIRECTOR FOR RESEARCH SERVICES, NATIONAL INSTITUTES OF HEALTH

COLLEEN F. BARROS, BUDGET OFFICER, OFFICE OF THE DIRECTOR, NATIONAL INSTITUTES OF HEALTH

DENNIS P. WILLIAMS, ACTING DEPUTY ASSISTANT SECRETARY, BUDGET, DEPARTMENT OF HEALTH AND HUMAN SERVICES

Chairman NATCHER. We take up next the Office of the Director, and Buildings and Facilities. We have before the Committee at this time Mr. Edward E. Nicholas, Jr., the Acting Associate Director for Administration.

Mr. Nicholas, who do you have there at the table with you?

Mr. NICHOLAS. Mr. Chairman, Dr. Raub, to Dr. Wyngaarden's right; Dr. Becker to my immediate left; and Ms. Barros, the OD Budget Officer.

Chairman NATCHER. We are delighted to have all of you.

Do you have a preliminary statement for us before we proceed with the questions?

Mr. NICHOLAS. Yes, I do, sir.

Chairman NATCHER. Go right ahead.

Mr. NICHOLAS. My testimony covers two appropriations that support all NIH programs: first, the appropriation for the Office of the Director which includes the Director and his staff who assist him in the administration and coordination of the NIH programs, and for administrative support functions, such as budget, accounting and personnel.

The appropriation request for 1987 for the Office of Director is $36.7 million. This request includes $10 million for the continuation of a program that supports biomedical research in small and minority schools and universities.

The second appropriation for which Dr. Becker and I are testifying is Buildings and Facilities. This appropriation provides funds for the design, construction, and repair and improvement of NIH facilities. Our request under this appropriation includes $3 million for the renovation and construction of animal holding facilities and $5 miilion for an ongoing program of routine repairs and improvements.

This is a brief summary, Mr. Chairman. I will be glad to answer any questions.

Chairman NATCHER. Thank you, Mr. Nicholas.

[Statement follows:]

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Statement by Acting Associate Director for Administration

Office of the Director

I am pleased to have the opportunity to discuss with the Committee the Office of the Director and the Buildings and Facilities appropriations of the NIH.

Office of the Director

This appropriation funds those components of the central administration that are primarily responsible for the development of NIH-wide policy and procedures and the coordination of program activities. The Immediate Office of the Director includes the principal associates of the Director and staff officers who provide advice and assistance in the administration and coordination of the intramural and extramural research programs of the Bureaus, Institutes and Divisions. Other offices provide leadership in such areas as equal opportunity, program planning and evaluation, disease prevention, medical applications of research, public and scientific communication, protection from research risks, management analysis and review, contracts and grant administration, and budget and personnel management.

Mr. Chairman, the appropriation request for 1987 for the Office of the Director is $36,701,000.

Buildings and Facilities

The second appropriation for which I am testifying is the Buildings and Facilities appropriation that provides funds for the design, construction, and repair and improvement of clinical and laboratory buildings and supporting facilities for the National Institutes of Health.

The appropriation request of $8,000,000 in fiscal year 1987 is for the following:

Animal Facilities Project: With increased public interest in the use and care of animals in research, NIH administration is concerned that its own facilities for housing and utilizing animals meet its own guidelines on animal use and care, as well as others that will be promulgated as the result of recently enacted legislation. Approximately 80 percent of NIH intramural animal holding space meets the standards of the American Association for Accreditation of Laboratory Animal Care, leaving 83,000 square feet of unaccredited space.

The NIH has established a goal of insuring that all animal facilities on the NIH campus meet the AAALAC standards by October 1987. Two phases of activities in this effort have been identified. The first phase, of two-year duration, would involve the consolidation of existing animal facilities within individual buildings, renovation of existing space, and new construction; the second phase, of 5 to 10 years, would require the greater consolidation of scattered animal holding activities and construction of new facilities. The 1987 request for $3,000,000 will permit progress under the first phase of this plan by allowing the consolidation of some of the existing animal facilities, renovation, and construction.

Repairs and Improvements: The Repairs and Improvements program applies to the main physical plant at Bethesda, Maryland and other field stations for which NIH is responsible. Activities supported with these funds are relatively small and unanticipated to the extent that lead time is not sufficient to request funds during the regular budget cycle. The request of $5,000,000 in FY 1987 will provide for the maintenance of our extensive physical plants and for changes related to program needs.

Thank you. I shall be happy to respond to any questions you may have.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

National Institutes of Health

Biographical Sketch

NICHOLAS, MR. EDWARD E. JR.
Acting Associate Director for Administration, NIH

October 20, 1923. Rock Island, Illinois.
Married, three children.

Education. A.B., Augustana College, 1949. M.S., Columbia University, 1950.

Professional History. 1950-1951, Salary & Wage Analyst, Rock Island Arsenal, Rock Island, Illinois. 1951-1952, Salary & Wage Chief and Assistant Personnel Officer, Pittsburgh Ordnance District, Pittsburgh, Pennsylvania. 1952-1955, Assistant Salary & Wage Chief, Ordnance Corps, Pentagon. 1955-1958, Salary & Wage Chief, Ordnance Corps, Pentagon. 1958-1962, Chief, Civilian Personnel Management Section, Ordnance Corps, Pentagon. 1962-1963, Personnel Management Specialist, NIH. 1963-1969, Chief, Personnel Staffing Branch, Office of Personnel Management, NIH. 1969-1974, Assistant Director for Operations, Office of Personnel Management, NIH. 1974-Present, Director, Division of Personnel Management, NIH. 1979-1980, Acting Associate Director for Administration, NIH. February 1986-Present, Acting Associate Director for Administration, NIH

Military Service. 1943-1946, United State Army, Office of Strategic Services.

Honors, Awards. Sustained Superior Performance Award, 1973. Superior Service Award, 1974. Public Health Service Special Recognition Award, 1981.

OD BUDGET REQUEST

Chairman NATCHER. Now, if you will, give us for the record a detailed breakdown by program of your 1987 budget request along with the figures for 1985 and 1986, and identify the amounts involved in sequestration, and proposed for rescission.

[The information follows:]

NATIONAL INSTITUTES OF HEALTH, OFFICE OF THE DIRECTOR—FY 1987 BUDGET REQUEST

[Dollars in thousands]

	1985 appropriation	1986 appropriation	1986 proposed recission	1986 sequestration	1986 estimate	1987 request
RCMI	$5,000	$10,000	−$4,570	−$430	$5,000	$5,000
Area	5,000	10,000	−4,570	−430	5,000	5,000
Other	28,304	26,992	0	−1,161	25,831	26,701
Total	38,304	46,992	−9,140	−2,021	36,831	36,701

Note: Figures for the 1986 Columns are comparable to 1985 and 1987, i.e., they exclude amounts for AIDS

AREA AWARDS

Chairman NATCHER. How much are you proposing for academic research enhancement award in 1987?

Mr. NICHOLAS. Dr. Raub?

Chairman NATCHER. Yes. Dr. Raub?

Dr. RAUB. The proposal for 1987, Mr. Chairman, is $5 million. That is the same amount as the revised proposal for 1986 and the same amount as fiscal year 1985.

Chairman NATCHER. Thank you.

If you will, give us a list of the 75 awards which were made in 1985. If you would place that in the record, we would appreciate it.

[Information follows:]

ACADEMIC RESEARCH ENHANCEMENT AWARDS

Institution Name (No. of Awards)
City and State

American University (1)
Washington, DC

Auburn University
at Auburn (1)
Auburn, AL

Ball State University (4)
Muncie, IN

Barnard College (1)
New York, NY

Benedict College (1)
Columbia, SC

Bennington College (1)
Bennington, VT

Bryn Mawr College (2)
Bryn, PA

California State
Polytech University (1)
Pomona, CA

California State Univer. (2)
at Long Beach
Long Beach, CA

California State Univer. (2)
at Northridge
Northridge, CA

California State Univer. (1)
at Fullerton
Fullerton, CA

Carleton College (1)
Northfield, MN

Clark University (2)
Worcester, MA

Clemson University (2)
Clemson, SC

Colgate University (1)
Hamilton, NY

New York State College
at Old Westbury (1)
Old Westbury, NY

College of Charleston (1)
Charleston, SC

New York State College
College of Techonlogy
Utica-Rome (1)
Utica, NY

Duquesne Univeristy (1)
Pittsburgh, PA

Eastern Michigan Univ. (1)
Ypsilanti, MI

Franklin and Marshall
College (1)
Lancaster, PA

Haverford College (1)
Haverford, PA

Kenyon College (2)
Gambier, OH

Lamar Univeristy (1)
Beaumont, TX

Louisiana State Univ.
Univ. of New Orleans (1)
New Orleans, LA

Luther College (1)
Decorah, IA

Manhattan College (2)
Bronx, NY

Memphis State Univer. (1)
Memphis, TN

Miami Univer. Oxford (2)
Oxford, OH

Mount Holyoke College (3)
South Hadley, MA

Murray State Univer. (1)
Murray, KY

Northern Kentucky Univ. (1)
Highland Heights, KY

Phillips University (1)
Enid, OK

Radford University (1)
Radford, VA

Ramapo College of New Jersey (1)
Mahwah, NJ

Rutgers The State Univ.
Camden (1)
Camden, NJ

Seton Hall University (1)
South Orange, NJ

Smith College (1)
Northhampton, MA

Southern Illinois Univ.
at Edwardsville (2)
Edwardsville, IL

Spelman College (1)
Atlanta, GA

St. John's University (1)
New York, NY

Swarthmore College (1)
Swarthmore, PA

Tuskegee University (1)
Tuskegee Institute, AL

University of Akron (3)
Akron, OH

University of Alabama
in University (1)
University, AL

University of Alabama
in Huntsville (1)
Huntsville, AL

University of Alaska
Anchorage (1)
Anchorage, AK

University of Colorado
at Denver (1)
Denver, CO

University of Kansas College
of Health Sciences & Hospital
School of Nursing (1)
Kansas City, KS

University of Kansas College
of Health Sciences & Hospital
School of Allied Health (1)
Kansas City, KS

University of Maine Orono (1)
Orono, ME

University of Nevada
Las Vegas (1)
Las Vegas, NV

University of Richmond (1)
Richmond VA

University of Texas
Arlington (1)
Arlington, TX

University of Texas
El Paso (1)
El Paso TX

University of Wisconsin (2)
Eau Claire, WI

Washburn University (1)
Topeka, KS

Wichita State University (1)
Wichita, KS

Chairman **Natcher**. How many applications for these research awards have you received?

Dr. **Raub**. In the only competition to date, which was last year, we received 423 applications. Of those, 75 received research grants.

RCMI AWARDS

Chairman **Natcher**. Now, under Research Centers in Minority Institutions, how much are you proposing for this program in 1987?

Dr. **Raub**. We also are proposing $5 million for that program in 1987, a continuation of the revised 1986 level and the 1985 level.

Chairman **Natcher**. If you will, give us a list of the grants which were made, in the record.

[Information follows:]

Research Centers in Minority Institutions (RCMI)

Florida A & M University, Tallahassee, Florida.
Meharry Medical College, Nashville, Tennessee.
Atlanta University, Atlanta, Georgia.
Howard University, Washington, D.C.
Hunter College, New York, New York.
City College of New York, New York, New York.
Ponce School of Medicine, Ponce, Puerto Rico.

AIDS

Chairman **Natcher**. Last year, $70 million was added by Congress to this account for research on AIDS. Please insert a table in the record showing which Institutes will receive these funds in 1986.

[Information follows:]

NATIONAL INSTITUTES OF HEALTH AIDS FUNDING SUMMARY, 1986 HISTORY

[Dollars in thousands]

	Appropriation	Sequestration	Rescission	Amounts available	Planned allocation	Current estimate
NCI	$28,441	−$1,223		$27,218	+13,450	$40,668
NHLBI	11,200	−482		10,718		10,718
NIDR	684	−29		655	+1,057	1,712
NINCDS	1,500	−65		1,435		1,435
NIAID	27,067	−1,164		25,903	+35,527	61,430
NEI	100	−4		96		96
DRR	1,731	−74		1,657		1,657
OD	70,000	−3,010	−13,915	53,075	−50,034	3,041
Total, NIH	140,723	−6,051	−13,915	120,757		120,727

Chairman **Natcher**. Does the Office of the Assistant Secretary for Health play any role in the allocation of these funds for 1986?

Dr. **Wyngaarden**. No, sir. We were given the freedom to allocate those funds with the exception that $20 million was subject to rescission and sequestration.

Chairman **Natcher**. All right.

Mr. Conte, I yield to you.

Mr. **Conte**. Thank you, Mr. Chairman.

It is good to see you, Mr. Nicholas, and to go over the overall administrative budget for NIH as well as wrap up our hearings on

NIH. I tell you, from where I sit, this budget has not been getting any easier. Year after year, it gets more difficult, and the climate gets more and more arid as we look at it.

LABORATORY AND CLINICAL CENTER MODERNIZATION

Doctor, last year you testified that the ten-year modernization plan for the clinical center and the campus research labs had gotten off schedule. Instead of seeing the funding completed within that ten-year period, starting in 1979, we are now likely to see requests coming up through 1993.

Is that still the case?

Mr. **Nicholas**. Yes. Dr. Becker?

Dr. **Becker**. That is, indeed, the case, Mr. Conte.

Mr. **Conte**. Why did we get so far off target?

Dr. **Becker**. It was just not possible to do all of the projects that needed to be done without tremendous disruptions at the Clinical Center.

Mr. **Conte**. It is not because of the money?

Dr. **Becker**. No, it really was not a money problem. The extension was primarily due to the disruption.

Mr. **Conte**. What do you have for an unexpended balance?

Dr. **Becker**. The only balance in that account now is about $11 million for the current year; but I should mention to you that we have one major project that you really have not heard about as part of the Clinical Center modernization. There is a letter underway to you and the Chairman through channels explaining this.

One of the plans in the Clinical Center modernization was to upgrade the existing heart and neurosurgery facilities that were built in the early 1960s. We found, as the modernization progressed that that particular wing of the building simply was not subject to upgrading without expenditures of approximately $11 million.

We have revised the program to utilize the funds available this year—about $7.4 million—to construct an addition to our cancer and eye surgery facilities that will provide space for cardiac and neurosurgery. The wing of the building that thus will be freed will then be used as animal facilities. This will aid in meeting the new animal standards requirements.

These activities will add to the length of the project. It will not extend beyond 1993, but it will utilize the funds this year that we might otherwise have used for other projects.

It is critical, however, that we do this.

Mr. **Conte**. Well, Dr. Nicholas, I will submit the balance of my questions for the record.

Chairman **Natcher**. Mr. Early?

Mr. **Early**. Just one quick point.

I am glad to see, Mr. Nicholas, you are trying to keep up with the AAALAC standard. Will you reach that goal?

Mr. **Nicholas**. Our target is for October of next year.

Mr. **Early**. I have some other questions that I will put in the record.

Thank you.

Chairman **Natcher**. Mr. Hoyer?

OFFICE OF RESEARCH SERVICES

Mr. Hoyer. I am not going to ask questions here, Dr. Becker. I have a number of questions that I want to submit. I would like relatively complete answers.

As you know, Mr. Stokes and I have some concerns that relate to the reorganization of the Office of Research Services and I am going to pursue those.

Obviously, time is of the essence here and we will not go into them now.

Dr. Becker. We will be glad to provide anything for the record or to discuss with you personally any of your concerns.

Mr. Hoyer. Presumably, we will pursue both avenues.

Thank you, sir.

Thank you, Mr. Chairman.

Chairman Natcher. Dr. Wyngaarden, for the record, if you will, please, supply a copy of your 1987 budget submission to the Public Health Service and the Department; also please provide for the record details of how you would use a $500 million increase over your 1987 budget in increments of $100 million.

Assume that Congress does not approve any of the proposed 1986 rescissions. Please, if you will, provide for the record a table showing, for competing research project grants for 1986/1987, the number, amount, pay line, award rate and average cost assuming that no limit is placed on indirect costs.

[The information follows:]

ALLOCATION OF ADDITIONAL FUNDS

Mr. Natcher: Also, please provide for the record details of how you would use a $500 million increase over your 1987 budget in increments of $100 million. Assume that Congress does not approve any of the proposed 1986 rescissions.

Dr. Wyngaarden: The tables on the following pages show how NIH would distribute an additional $500 million in increments of $100 million above the FY 1987 President's budget request. The components of each increment are listed below.

1st Increment

- Provides an additional 549 noncompeting awards due to the funding of 6,073 competing research project grants in FY 1986 in lieu of the 5,492 grants proposed at the FY 1986 rescission level.
- Provides additional support for the upgrading of all NIH intramural animal facilities to achieve accreditation standards set by the American Association for Accreditation of Laboratory Animal Care (AAALAC).
- Provides partial support for the 9th year of the Clinical Center modernization program.
- Provides an approximate current services level for intramural research.
- Provides funds to begin to address the needs for small instrumentation. A recent survey has identified many problem areas concerning obsolete or poorly maintained research instrumentation. The most significant need cited by the survey is the need for relatively low cost pieces of equipment in the price range of $5,000 to $60,000.
- Provides partial support for restoration of the research centers program to the FY 1986 funding level.
- Provides an additional 47 research trainees for a total of 9,305.

2nd Increment

- Reduces the rate of downward negotiation in noncompeting research project grants from 10.3 percent to 9.2 percent.
- Provides an additional 121 competing research project grants for a total of 5,225.
- Reduces the rate of downward negotiation in competing research project grants from 13.3 percent to 12.2 percent.
- Provides modest program expansion in the intramural research program.

- Provides additional support for the 9th year of the Clinical Center modernization program.

- Provides support for the planning of the Child Health/ Neurosciences building.

- Provides additional support for the small instrumentation program.

- Provides additional support for partial restoration of the research centers program to the FY 1986 funding level.

- Provides an additional 235 research trainees for a total of 9,540.

- Provides an approximate current services level for research career awards.

- Provides the Division of Computer Research and Technology increased support for projects related to vector processing, laboratory workstations and networking.

- Provides additional support for restoration of research and development contracts to approximately the FY 1986 funding level.

- Provides the small and minority universities and colleges program an increase to partially restore the program to the FY 1986 level.

- Provides an approximate current services level for the Cancer Control program.

- Provides current services and a small program increase to the National Library of Medicine.

3rd Increment

- Reduces the rate of downward negotiation in noncompeting research project grants from 9.2 percent to 7.8 percent.

- Provides an additional 100 competing research project grants for a total of 5,325.

- Reduces the rate of downward negotiation in competing research project grants from 12.2 percent to 10.8 percent.

- Provides increased support for the intramural research program.

- Provides additional support for the small instrumentation program.

- Provides additional support for partial restoration of research centers program to the FY 1986 funding level.

- Provides a funding level for research and development contracts slightly below current services.
- Provides modest support for the extramural construction program.
- Provides an additional 122 research trainees for a total of 9,662.
- Provides the small and minority universities and college program an increase to partially restore program to the FY 1986 level.
- Provides support for several new clinical trials.
- Provides additional funds for DRR's extramural animal facilities.

4th Increment

- Reduces the rate of downward negotiation in noncompeting research project grants from 7.8 percent to 6.4 percent.
- Provides an additional 125 competing research project grants for a total of 5,450.
- Reduces the rate of downward negotiation in competing research project grants from 10.8 percent to 9.7 percent.
- Provides additional support for the intramural research program.
- Provides additional support for the restoration of the research centers program to the FY 1986 funding level.
- Provides an additional 216 research trainees for a total of 9,878.
- Provides an approximate current services level for research and development contracts.
- Provides the small and minority universities and colleges program an increase to partially restore program to the FY 1986 level.
- Provides additional support for several new clinical trials.
- Provides additional support for the research management and support program.
- Provides funds to partially cover operating cost increases in the Office of the Director.

5th Increment

- Reduces the rate of downward negotiation in noncompeting research project grants from 6.4 percent to 4.8 percent.

- o Provides an additional 150 competing research project grants for a total of 5,600.
- o Reduces the rate of downward negotiation in competing research projects grants from 9.7 percent to 8.3 percent.
- o Provides enhanced support for the intramural research program.
- o Provides additional support to restore the research centers program to the FY 1986 level with a small increase in average costs.
- o Provides an additional 122 research trainees for a total of 10,000.
- o Provides the small and minority universities and colleges program an increase to restore the program to its approximate FY 1986 level.
- o Provides additional support for several new clinical trials.
- o Provides for modest increases in the research management and support program.
- o Provides additional funds to partially cover operating cost increases in the Office of the Director.
- o Provides support for design of facilities to replace currently leased research facilities at the National Institute of Environmental Health Sciences.

This revised estimate of $5,436.2 million excludes all NIH funding for Acquired Immune Deficiency Syndrome (AIDS) activities consistent with the Administration's proposal to centralize all AIDS funding in the Office of the Assistant Secretary for Health appropriation.

This estimate also assumes implementation of the Administration's indirect cost proposal on October 1, 1987.

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(Dollars in Thousands)

	FIRST $100,000 INCREMENT	SECOND $100,000 INCREMENT	THIRD $100,000 INCREMENT	FOURTH $100,000 INCREMENT	FIFTH $100,000 INCREMENT	TOTAL $500,000
# Competing	5104	5225	5325	5450	5600	
Nonc. Avg. Down. Neg.	-10.3%	-9.2%	-7.8%	-6.4%	-4.8%	
Comp. Avg. Down. Neg.	-13.3%	-12.2%	-10.8%	-9.7%	-8.3%	
Total Avg. Down. Neg.	-11.1%	-10.0%	-8.7%	-7.4%	-5.9%	
Award Rate	27.4%	28.1%	28.6%	29.3%	30.1%	
Payline	160-165	160-165	160-165	160-165	166-170	
Noncompeting RPGs	$74,000	$24,764	$32,241	$32,240	$36,845	$200,090
Competing RPGs	---	27,836	27,759	28,760	36,155	120,510
Subtotal, RPGs	74,000	52,600	60,000	61,000	73,000	320,600
E&F, Animal Fac.	10,000	---	---	---	---	10,000
E&F, Clin.Center Mod.	2,000	3,000	---	---	---	5,000
Intramural Res.	9,000	9,000	9,000	9,000	9,000	45,000
Instrumentation	2,000	5,000	5,000	---	---	12,000
Research Centers	2,000	5,000	5,000	5,000	5,000	22,000
Res. Training	1,000	5,000	2,500	4,500	2,500	15,500
Res. Careers	---	3,000			---	3,000
DCRT	---	1,000	---	---	---	1,000
R&D Contracts	---	5,000	5,000	5,000	---	15,000
E&F, C.H./Neuro.Plan	---	4,400	---	---	---	4,400
RCMI/ARFA	---	3,000	2,000	2,000	2,000	9,000
NCI, Cancer Control	---	2,000	---	---	---	2,000
NLM	---	2,000	---	---	---	2,000
Extramural Const.	---	---	5,000	---	---	5,000
Clinical Trials	---	---	3,500	10,000	4,500	18,000
Extramural Animal Fac.	---	---	3,000	---	---	3,000
RMS	---		---	3,000	2,000	5,000
OD	---	---		500	500	1,000
E&F, NIEHS Repl. Fac.		---		---	1,500	1,500
Subtotal, Other	26,000	47,400	40,000	39,000	27,000	179,400
TOTAL	100,000	100,000	100,000	100,000	100,000	500,000

DHHS NATIONAL INSTITUTES OF HEALTH

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(Dollars in Thousands)

BID	FY 1986 After Sequestration Comparable	FY 1987 Request	1st $100 Million		
			Noncompeting RPGs Denial of FY 1986 Rescission	B&F Animal Facilities	B&F Clin. Center Modernization
NCI	$1,174,225	$1,158,084	$11,097	---	---
NHLBI	911,544	795,837	[illegible]		---
NIDR	98,101	96,482	0		---
NIDDK	436,147	418,971	6,911		---
NINCDS	411,024	399,551	5,294		---
NIAID	341,297	330,551	7,424		
NIGMS	493,764	471,512	10,563		---
NICHD	288,269	284,119	1,365		---
NEI	186,598	179,200	2,716		
NIEHS	188,883	187,405	0		---
NIA	150,446	145,829	3,172	---	---
NIAMSD	111,117	106,732	3,072	---	---
DRR	298,751	274,192	---	---	---
FIC	10,895	11,205			---
NLM	[illegible]	56,400			---
OD	44,965	[illegible]	---		---
B&F	14,259	6,000		10,000	2,000
Total	[illegible]	[illegible]	[illegible]	10,000	2,000

1st $100 Million, 000s

BID	Extramural Research	Small Instrumentation	Research Centers	Research Training	Subtotal 1st Increment
NCI	[illegible]	[illegible]	$0	$144	$14,540
NHLBI	[illegible]	[illegible]	[illegible]	100	14,0[illegible]
NIDR	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
NIDDK	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
NINDS	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
NIAID	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
NIGMS	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
NICHD	[illegible]	[illegible]	[illegible]	[illegible]	7,432
NEI	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
NIEHS	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
NIA	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
NIAMS	[illegible]	34	[illegible]	[illegible]	[illegible]
DRR	[illegible]	[illegible]	[illegible]	[illegible]	0
FIC	[illegible]	[illegible]	[illegible]	0	0
NLM	[illegible]	[illegible]	[illegible]	0	0
OD	[illegible]	[illegible]	[illegible]	0	0
ERI	[illegible]	[illegible]	[illegible]	0	12,000
Total	[illegible]	[illegible]	[illegible]	[illegible]	100,000

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Allocation of an Additional $500 Million
by Institute and by $100 Million Increments, Cont.
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2nd $100 Million

BID	Noncompeting RPGs (Negotiations)	Competing RPGs (Add. Projects & Negotiations)	B&F Clin. Center Mod.	Intramural Research	Small Instrumentation	Research Centers	Research Training
NCI.....	$1,778	$7,700	[illegible]	$3,117	$959	$0	$720
NHLBI..	1,641	7,393	[illegible]	952	890	1,946	900
NIDR....	0	555	[illegible]	332	77	418	105
NIDDK...	5,764	2,047	[illegible]	819	519	164	455
NINCDS.	6,200	4,312	[illegible]	783	481	685	315
NIAID..	1,570	3,292	[illegible]	843	410	503	240
NIGMS.	2,835	1,900	[illegible]	0	703	888	1,325
NICHD	270	1,041	[illegible]	565	330	30	310
NEI.....	2,726	2,013	[illegible]	374	345	122	125
NIEHS.	[illegible]	153	[illegible]	862	94	68	260
NIA.	494	46	[illegible]	337	150	56	130
NIAMDD	1,498	594	[illegible]	101	124	121	115
DRR	[illegible]	[illegible]	[illegible]	0	0	0	0
FIC		[illegible]	[illegible]	0	0	0	0
NLM			[illegible]	0	0	0	0
OD			[illegible]	0	0	0	0
B&F		[illegible]	5,000	0	0	0	0
Total	24,764	31,836	5,000	9,000	5,000	5,000	5,000

2nd $100 Million, Cont.

BID	Research Careers	DCRT	R&D Contracts	B&F C.H./Neuro. Bldg. Plan	RCMI/ AREA	Cancer Control	NLM	Subtotal 2nd Increment
NCI	$209	$418	$347	---	---	$2,000	---	$17,248
NHLBI	691	103	135	---	---	---	---	14,655
NIDR	128	37	12	---	---	---	---	1,464
NIDDK	607	81	423	---	---	---	---	10,379
NINCDS	361	71	1,042	---	---	---	---	14,250
NIAID	121	68	2,164	---	---	---	---	7,121
NIGMS	0	10	3	---	---	---	---	7,744
NICHD	176	60	57	---	---	---	---	2,875
NEI	250	23	19	---	---	---	---	4,290
NIEHS	141	61	192	---	---	---	---	1,873
NIA	180	43	586	---	---	---	---	1,999
NIAMSD	104	6	7	---	---	---	---	3,638
DRR	32	7	13	---	---	---	---	52
FIC	0	1	0	---	---	---	---	1
NLM	0	4	0	---	---	---	2,000	2,004
OD	0	7	0	---	3,000	---	---	3,007
B&F	0	0	0	4,400	---	---	---	7,400
Total	3,000	1,000	5,000	4,400	3,000	2,000	2,000	100,000

DHHS-NATIONAL INSTITUTES OF HEALTH

Allocation of an Additional $500 Million
by Institute and by $100 Million Increments, Cont.
(Dollars in Thousands)

3rd $100 Million

BID	Noncompeting RPGs (Negotiations)	Competing RPGs (Add. Projects & Negotiations)	Intramural Research	Small Instrumentation	Research Centers	R&D Contracts
NCI.....	$4,082	$7,078	$3,117	$959	$0	$2,014
NHLBI...	5,724	5,668	952	890	1,946	781
NIDR....	486	502	332	77	418	69
NIDDK...	3,864	2,106	819	519	164	132
NINCDS..	3,509	4,179	783	481	685	188
NIAID...	3,142	1,805	843	410	503	261
NIGMS...	5,070	2,165	0	703	888	19
NICHD...	2,047	1,632	585	338	38	333
NEI.....	1,850	925	274	245	121	108
NIEHS...	496	522	862	94	68	783
NIA.....	974	665	332	150	38	198
NIAMSD..	1,047	711	101	134	131	38
DRR.....	---	---	0	0	0	76
FIC.....	---	---	0	0	0	0
NLM.....	---		0	0	0	0
OD......	---	---	0	0	0	0
B&F.....	---		0	0	0	0
Total...	32,241	27,759	9,000	5,000	5,000	5,000

3rd $100 Million, Cont.

BID	Extramural Const.	Research Training	RCMI/ AREA	Extramural Animal Facilities	Clinical Trials	Subtotal 3rd Increment
NCI.....	$2,000	$240	---	---	$1,387	$20,877
NHLBI....	1,500	270	---	---	480	18,211
NIDR....	---	43	---	---	0	1,927
NIDDK....	---	160	---	---	292	8,056
NINCDS....	---	105	---	---	626	10,556
NIAID....	---	72	---	---	102	6,938
NIGMS....	---	1,287	---	---	0	10,132
NICHD....	---	105	---	---	259	5,336
NEI.....	1,500	50	---	---	354	5,427
NIEHS....	---	72	---	---	0	2,897
NIA.....	---	52	---	---	0	2,359
NIAMSD....	---	46	---	---	0	2,208
DRR.....	---	0	---	2,000	0	3,076
FIC.....	---	0	---	---	0	0
NLM.....	---	0	---	---	0	0
OD.....	---	0	2,000	---	0	2,000
B&F.....	---	0	---	---	0	0
Total	5,000	2,500	2,000	2,000	3,500	100,000

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Allocation of an Additional $500 Million
by Institute and by $100 Million Increments, Cont
(Dollars in Thousands)

4th $100 Million

BID	Noncompeting RPGs (Negotiations)	Competing RPGs (Add. Projects & Negotiations)	Intramural Research	Research Centers	Research Training
NCI.....	$4,082	$6,512	$3,117	$0	$528
NHLBI...	[illegible]	[illegible]	952	1,946	630
NIDR...	486	475	[illegible]	[illegible]	85
NIDDK.	[illegible]	3,426	[illegible]	164	342
NINCDS.	[illegible]	[illegible]	[illegible]	685	231
NIAID.	3,142	[illegible]	[illegible]	503	368
NIGMS..	[illegible]	[illegible]	0	[illegible]	1,817
NICHD..	[illegible]	1,862	385	38	227
NEI.	[illegible]	1,268	274	121	105
NIEHS.	394	[illegible]	867	68	176
NIA..	[illegible]	[illegible]	222	78	104
NIAMSD.	[illegible]	774	201	151	92
DRR.			0		0
FIC.			0	0	0
NLM.			0	0	0
OD.			0	0	0
B&F			0	0	0
Total	[illegible]	29,768	[illegible]	5,000	4,500

4th $100 Million, Cont.

BID	R&D Contracts	RCMI/ AREA	Clinical Trials	Research Mgmt. & Support	Office of the Director	Subtotal 4th Increment
NCI......	$2,014	---	$3,961	$821	---	$21,035
NHLBI...	781	---	1,372	503	---	17,087
NIDR....	59	---	0	95	---	1,964
NIDDK...	132	---	834	209	---	9,290
NINCDS..	169	---	1,709	232	---	10,745
NIAID...	262	---	297	223	---	7,310
NIGMS...	19	---	0	180	---	10,729
NICHD...	[illegible]	---	240	212	---	6,044
NEI.....	110	---	1,012	86	---	4,815
NIEHS...	143	---	0	82	---	2,816
NIA.....	199	---	0	116	---	2,408
NIAMSD..	28	---	[illegible]	42	---	2,190
DRR.....	2	---	0	121	---	199
FIC.....	0	---	0	68	---	68
NLM.....	0	---	0	0	---	0
OD......	0	2,000	0	0	500	2,500
B&F.....	0	---	0	0	---	0
Total...	5,000	2,000	10,000	3,000	500	100,000

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Allocation of an Additional $500 Million
by Institute and by $100 Million Increments, Cont.
(Dollars in Thousands)

5th $100 Million

BID	Noncompeting RPGs (Negotiations)	Competing RPGs (Add. Projects & Negotiations)	Intramural Research	Research Centers	Research Training	RCMI/ AREA
NCI......	$4,662	$5,209	$7,110	$684	$240	---
NHLBI......	6,342	[illegible]	452	1,117	270	
NIDR......	559	556	232	206	47	---
NIDDK......	4,414	[illegible]	613	279	360	
NINCDS......	4,009	4,072	183	345	105	---
NIAID......	[illegible]	2,268	843	110	72	
NIGMS......	[illegible]	5,547	0	262	1,281	
NICHD......	2,340	2,368	540	226	193	
NEI......	[illegible]	1,156	174	76	50	---
NIEHS......	566	543	662	187	52	---
NIA......	1,956	[illegible]	220	43	53	
NIAMSD......	1,196	914	131	111	46	---
DRR......			0	1,262	0	---
FIC......			0	0	0	---
NLM......			0	0	0	
OD......			0	0	0	2,000
B&F......			0	0	0	---
Total......	36,845	36,155	[illegible]	5,000	1,500	2,000

5th $100 Million, Cont.

BID	Clinical Trials	B&F NIEHS Repl. Fac.	Research Mgmt. & Support	Office of the Director	Subtotal 5th Increment	TOTAL FY 1987 Rev. Est.
NCI......	$1,356	---	$551	---	$18,719	$1,250,558
NHLBI...	618	---	337	---	17,155	868,502
NIDR....	85	---	64	---	1,881	104,190
NIDDK...	376	---	328	---	9,788	466,510
NINCDS.	805	---	156	---	10,324	452,144
NIAID.	131	---	150	---	7,328	367,716
NIGMS.	0	---	126	---	11,036	530,638
NICHD.	333	---	142	---	6,099	331,895
NEI.	455	---	57	---	4,614	201,442
NIEHS.	0	---	55	---	2,442	198,796
NIA.	0	---	71	---	2,485	158,668
NIAMSD.	341	---	28	---	2,737	120,793
DRR.	0	---	63	---	3,346	238,865
FIC.	0		46		46	11,420
NLM.	0		0		0	56,412
OD.	0	---	0	500	2,500	46,708
B&F.	0	1,500	0		1,500	28,900
Total.	4,500	2,500	2,000	500	100,000	5,436,157

Chairman **Natcher**. Dr. Wyngaarden, this concludes the hearings for the National Institutes of Health for the fiscal year 1987 budget. These have been good hearings, Doctor.

As I said out at the National Institutes of Health not too long ago, the people at NIH are able people, Dr. Wyngaarden. It is a pleasure for us on this Subcommittee to sit here and hear all of you testify and present your budget requests for the fiscal year 1987.

It has been that way ever since I have been a member of the Committee and this is no exception to the rule. Your budget requests have been well presented, Dr. Wyngaarden; and we want to thank you personally.

Mr. **Wyngaarden**. Thank you, Mr. Natcher.

On behalf of all the directors and others who have testified, we want to thank you and the members of the Committee for this very careful regard of our programs and activities.

We are much indebted to you.

Chairman **Natcher**. Thank you very much.

The Committee will now adjourn until 10:00 in the morning.

[The following questions were submitted to be answered for the record:]

ACADEMIC RESEARCH ENHANCEMENT AWARD

Mr. Natcher. Please describe the procedures for review and approval of the AREA awards.

Dr. Raub. AREA grant applications are reviewed in accordance with the peer review regulations which govern the evaluation of all research applications submitted to the National Institutes of Health (NIH). Under these regulations, AREA applications are initially reviewed by panels of experts, referred to as study sections or initial review groups, which are established according to scientific disciplines. As a general policy, study sections that review AREA applications will include at least one member who represents an AREA-eligible institution. These panels of experts render an impartial review and evaluation of each application. They consider not only the scientific merit of a proposal, but also the background and experience of the principal investigator, the research facilities available for the project, and the appropriateness of the budget estimate. The reviewers recommend approval, disapproval, or deferral of an application. Recommendations for approval are accompanied by a "priority score," which confers a numerical ranking for the scientific merit of each application. Priority scores range from 100 to 500. One hundred denotes the highest of 500 the lowest scientific merit of an application recommended for approval.

Generally, all grant applications are then submitted to the national advisory council or board of the appropriate Institute for the second level of review. Since the recent enactment of the Health Research Extension Act of 1985 (P.L> 99-158), which authorizes NIH to make, without national advisory council review, grant awards whose annual direct costs are $50,000 or less, Institutes may make AREA grants without submitting the applications to their councils.

The director of an Institute may award an AREA grant only from among those applications that have been recommended for approval by the initial review group and the council (if council review took place).

Mr. Natcher. What are the terms and conditions of these awards?

Dr. Raub. AREA grants provide up to $50,000 in direct costs (plus applicable indirect costs) for a period not to exceed 24 months. These grants, which are non-renewable, may be administratively transferred to a replacement grantee institution only if the replacement is also an AREA-eligible institution.

RESEARCH CENTERS IN MINORITY INSTITUTIONS

Mr. Natcher. Please describe the procedures for review and approval of the RCMI grants.

Dr. Raub. After an initial screening by the ad hoc RCMI Review Committee, a committee of peers constituted solely for the review of RCMI applications, each applicant institution was site visited. The ad hoc RCMI Review Committee, using the site visit reports, the submitted applications, and any additional information which the applicants made available, evaluated each application and assigned a priority score to each. The National Advisory Research Resources Council of the Division of Research Resources concurred with the Review Committee's recommendations. These recommendations served as the basis for the FY 1985 awards.

Mr. Natcher. How many applications for these grants have you received?

Dr. Raub. Sixteen institutions met the eligibility criteria for the program--predominantly minority institutions which offer doctoral degrees in the health professions or the sciences related to health. Of the 16, all submitted RCMI applications in Fiscal Year 1985, and all 16 were recommended for approval.

Mr. Natcher. What are the terms and conditions of the RCMI grants?

Dr. Raub. Each RCMI grantee is expected to strengthen its research environment in order to expand the National capability for research in the health sciences. RCMI awards are intended to enhance significantly the capacity for the conduct of biomedical and/or behavioral research at minority institutions by strengthening their research environment. The Program can foster faculty expansion and enrichment, physical facility improvement, and other research related activities including laboratory renovation and equipment replacement.

MODERNIZATION OF FACILITIES

Mr. Conte. The $3 million that has been requested for animal facility modernization, is that part of the 10 year modernization plan, or is this a new initiative brought about by recent events?

Dr. Becker. This is a new initiative. The care given to research animals at NIH is very good, and over 80 per cent of our animal holding space meets the standards in the _NIH Guide lines for Care and Use of Laboratory Animals_ and has been accredited by the American Association for Accreditation of Laboratory Animal Care (AAALAC). However, 83,000 square feet of animal holding space on the NIH campus cannot meet AAALAC standards without renovation. For the last decade NIH has been committed to ultimate accreditation of all our animal facilities. Last summer the Director, NIH, established a goal of insuring that all such space is accreditable by the beginning of FY 1988. The $3 million requested will help meet that goal by permitting us to develop some of the new and upgraded animal facilities that are required.

Mr. Conte. One of the reasons I get concerned about the 10 year plan slipping is that it gets hard to figure when you are going to get to the Child Health building. I'm not sure that I fully understood the answer I got from the Child Health Institute on the $500,000 we provided in FY 1985 to update the plans for the building. Has that money been spent or not, and if it hasn't, will it be spent in FY 1986?

Dr. Becker. We have done a considerable amount of work on this project with our own staff, but we have not yet obligated the $500,000 that you provided for architectural design. Last summer we completed a stringent selection process of an architect-engineer (A/E) firm to carry out the design and a construction management firm to work with the A/E in planning the logistics of the construction process. As a result of Dr. Wyngaarden's initiative on improving our animal facilities on a priority basis, we deferred letting final contracts with these firms, since I felt that the proposed NICHD building should be integrated with these other plans. During the last two months it has become apparent that we can meet AAALAC accreditation standards by 1988, but for primates this will be only on an interim basis. In the long run, a new state-of-the-art facility for housing primates in close proximity to laboratories, especially in the neurosciences, will be needed.

As Dr. Alexander testified in the NICHD presentation, we believe that we can move ahead with the NICHD building and incorporate adequate primate and neuroscience research facilities, not only for NICHD, but for other Institutes involved in such research. We plan to ask the A/E to develop a program of requirements for an integrated NICHD/ neuroscience/ primate facility and then to provide us with concept designs and detailed cost estimates for the building. Thus we will obligate this year the funds that have been provided, probably in stages as the A/E completes individual tasks.

Mr. Conte. Where do you put the priority on a new Child Health Building, Dr.?

Dr. Becker. We continue to view the Child Health building, as modified to include additional neuroscience and primate facilities, as our top priority for laboratory construction.

Mr. Conte. Last year, when we were putting our FY 1986 conference report through the House, we ended up having to take an additional $3 million in cuts, $93,000 of which was to come out of the Office of the Director. How did you accommodate that reduction? How much more did Gramm-Rudman-Hollings take out, and what did that do to your operation?

Mr. Nicholas. The reduction of $93,000 was applied to non-personal services expenses. The Gramm-Rudman-Hollings reduction was $.9 million to the AREA and RCMI Programs and $1.2 million to the OD operating expenses. This was accommodated by applying across-the-board cuts to all personnel and non-personnel costs.

ACQUIRED IMMUNE DEFICIENCY SYNDROME

Mr. Conte. Also in that bill was the $70 million additional we added to the NIH research budget, doubling the budget request, which we placed in the Office of the Director. Assuming we don't put the money into the Office of the Assistant Secretary for Health as requested, but rather keep the money at the NIH level, should we adopt a similar approach in our FY 1987 bill, or should we divvy up all the funds among the institutes?

Dr. Wyngaarden. As an alternative to OASH centralization, it is my professional judgment that the concept of placing a portion of AIDS funding in the OD appropriation is an excellent approach to meeting the needs of the NIH program. The availability of an undistributed "pool" of resources permits much-needed flexibility in responding to emerging opportunities.

INDIRECT COSTS

Mr. Conte. As we have gone along in these hearings, as a result of the questions that all the members have asked, I think we've pieced together some of the answers of the indirect cost issue. It appears that HHS is the only agency that will implement the new proposed policy in FY 1986, and it also appears that this new policy could cause substantial reductions in payments to universities, even though no budgetary savings are assumed in your budget for FY 1986.

There is one other piece of the puzzle I'm still trying to figure out. As I understand it, the change in indirect costs will affect only universities, while no changes will be directed at other institutions like hospitals or private foundations. This would seem to create a strange situation where, if a grant goes to a place like Harvard, the indirect costs would be cut, whereas, if it goes to Massachusetts General Hospital, it would not. Is that correct, and what is the rationale behind this distinction?

Dr. Raub. The proposed changes in indirect cost policy emanate from two studies on the issue, one conducted by the White House Office of Science and Technology Policy (OSTP) and the other by the Department of Health and Human Services, Office of the Inspector General. The Office of Management and Budget (OMB) has proposed revisions to the cost principles for educational institutions (OMB Circular A-21) which would cap indirect cost reimbursement for administrative costs at the five year national average of 26%; projected to go into effect July 1, 1986. Since this is a limitation based on the current national average, there are no immediate projected savings for FY 86. An analysis of the effects of this change in FY 87 when the limit for administrative costs will be reduced to 20% suggests that the potential savings for all of the Public Health Service may be approximately $90 million dollars.

These proposed changes are occurring first within the cost principles for educational institutions because of the historical dollar growth in administrative cost categories such as departmental administration; a category of expense which is not entirely comparable in non-educational institutions.

ANIMAL FACILITIES

Mr. Conte. What part of your operation is now in charge of inspecting animal facilities?

Dr. Wyngaarden. The Office for Protection from Research Risks, (OPRR), within the Office of the Director of the National Institutes of Health, is responsible for conducting site visits in accordance with the recently revised Public Health Service Policy on the Humane Care and Use of Laboratory Animals. These visits may be announced or unannounced and may occur:

(a) to negotiate an institution's Animal Welfare Assurance,

(b) to assess an intitution's compliance with its Animal Welfare Assurance, and/or,

(c) to assess an institution's alleged noncompliance with Public Health Service animal welfare policy.

The Office of the NIH Deputy Director for Extramural Research and Training (OERT) conducts random site visits to institutions with approved Animal Welfare Assurances to assess the assurance mechanism as a means of ensuring appropriate and humane care and use of laboratory animals.

It is important to recognize that when site visits are conducted by OPRR or OERT an "inspection of facilities" is but one aspect of an overall evaluation of an institutions entire program for the care and use of laboratory animals. Other aspects of an institution's program that receive considerable scrutiny include the availability and qualifications of the individuals who provide veterinary care, the qualifications and training of other laboratory animal care personnel, the functions, responsibilities, and efficiency of the institutional animal care and use committee, procedures for emergency veterinary care and for quarantine and surgery of animals, the occupational health program for personnel who have contact with animals, and the access of veterinarians to all animals. Finally, and most importantly, the suitability of the administrative structure at the institution to operate a sound animal care and use program is closely examined. These aspects of an institutional program can only be evaluated by meeting with and asking questions of administrators, veterinarians, animal care and use committee members, researchers, animal technicians and animal caretakers, and by an extensive review of documents, procedures, minutes, protocols, and individual clinical health records of animals.

Mr. Conte. How often do you inspect animal facilities at NIH grant-receiving institutions?

Dr. Wyngaarden. Site visits are conducted by OPRR as needed for the reasons provided above. The OERT series of site visits includes approximately ten per year. As needed, Initial Review Groups (peer review) conduct research project site visits. Where animals are involved in the project, site visitors review the care and use of those animals involved in the project and report their findings to OPRR.

NIH also relies on the USDA Animal Plant Health Inspection Service (APHIS) inspections of institutions in accordance with the Animal Welfare Act. Institutions that APHIS finds to be in violation of the Animal Welfare Act are reported to NIH. The APHIS inspections are done on a routine basis at all institutions that fall within the purview of the Animal Welfare Act.

Mr. Conte. After the closing of three facilities that I am aware of, do you have a handle on how adequate animal care is, and how many such animal facilities might be subject to closing under current policy?

Dr. Wyngaarden. Based on the findings of 15 site visits to randomly selected institutions across the country, where no significant problems were found, we believe that most institutions are committed to proper care and use of laboratory animals and are fully capable of meeting the requirements for an adequate institutional program. Approximately 700 institutions hold Animal Welfare Assurances under the PHS Policy, and we do not find closings at three facilities to represent a significant portion of the total number of institutions. Nor do we believe that the three facilities where grant funds were suspended are representative of the kinds of institutional programs that exist throughout the country.

Problems that we have found in the past, and consider to be of a serious nature, include inactive and ineffective institutional animal care and use committees, loosely organized programs without effective administrative structures and well-defined responsibilities, and lack of procedures and mechanisms for solving day-to-day problems that occur in any program. The recently revised PHS Policy specifically addresses these problems and requires institutions to detail in their Animal Welfare Assurance documents information describing these problems if they exist. Although we do not anticipate finding many instances of these kinds of problems, some institutions will need guidance in developing an acceptable program. Generally, problems, even at institutions where grant funds have been suspended, have been corrected within a reasonably short period of time.

Mr. Conte. What does the need to upgrade animal facilities mean in terms of cost and impact on funds that would otherwise be used for instrumentation?

Dr. Wyngaarden. Projects requiring major instrumentation resources are seldom the same projects requiring major animal facility improvement. Choosing between instrumentation resources and animal resources is not a special decision in resource allocation. It is no different than choosing between animal facilities and clinical facilities or between animal facilities and the library.

Large sums of money have recently been made available for research institutions to upgrade, replace and improve their instrumentation. Much lesser amounts have been available to improve animal facilities.

The Congress has expressed concern for the well being of laboratory animals in two recent legislative actions, P.L. 99-158, the NIH reauthorization, and P.L. 99-198, the Amendments to the Animal Welfare Act. Complying with these laws will require some improvement in animal facilities at grantee institutions. A survey of the national laboratory animal situation in 1978 revealed a need to improve about one-third of the animal facilities and to replace about one-fourth of them. It is unlikely that this situation has improved. The National Academy of Sciences' Institute of Laboratory Animal Resources will carry out another survey and update the 1978 data in the coming year. It is expected that their fundings will indicate a need for approximately $100 million to improve animal facilities.

AREA/RCMI

Mr. Conte. We talked about one of the new programs funded through the Office of the Director yesterday dealing with the minority institutions. The other is the Academic Research Enhancement Awards, providing funds to undergraduate institutions that normally do not get many NIH grants. I believe my colleges in Western Massachusetts like Mt. Holyoke, did very well under the first round. How many awards did you make with the $5 million in FY 1985? For the record, will you provided a list of the awards?

Dr. Raub. A total of 75 AREA grants were awarded from the FY 85 appropriation of $5 million. The following provides the names of those institutions receiving awards and the number and dollar amount of the grants:

ACADEMIC RESEARCH ENHANCEMENT AWARDS

Institution City and State	Area Award No.	Area Award Amount
American University Washington, DC	1	60,404
Auburn University at Auburn Auburn, AL	1	59,332
Ball State University Muncie, IN	4	252,997
Barnard College New York, NY	1	85,299
Benedict College Columbia, SC	1	66,991
Bennington College Bennington, VT	1	59,088
Bryn Mawr College Bryn, PA	2	153,591
California State Polytech University Pomona, CA	1	63,572
California State Univer. at Long Beach Long Beach, CA	2	130,224
California State Univer. at Northridge Northridge, CA	2	128,611
California State Univer. at Fullerton Fullerton, CA	1	61,735
Carleton College Northfield, MN	1	77,413
Clark University Worcester, MA	2	146,677

Clemson University Clemson, SC	2	149,338
Colgate University Hamilton, NY	1	53,350
New York State College at Old Westbury Old Westbury, NY	1	58,459
College of Charleston Charleston, SC	1	81,926
New York State College College of Techonlogy Utica-Rome Utica, NY	1	63,500
Duquesne Univeristy Pittsburgh, PA	1	78,538
Eastern Michigan Univ. Ypsilanti, MI	1	63,608
Franklin and Marshall College Lancaster, PA	1	64,649
Haverford College Haverford, PA	1	59,035
Kenyon College Gambier, OH	2	144,489
Lamar Univeristy Beaumont, TX	1	51,808
Louisiana State Univ. Univ. of New Orleans New Orleans, LA	1	67,860
Luther College Decorah, IA	1	63,495
Manhattan College Bronx, NY	2	140,581
Memphis State Univer. Memphis, TN	1	71,500
Miami Univer. Oxford Oxford, OH	2	126,207
Mount Holyoke College South Hadley, MA	3	219,409
Murray State Univer. Murray, KY	1	61,096

Northern Kentucky Univ. Highland Heights, KY	1	79,451
Phillips University Enid, OK	1	63,496
Radford University Radford, VA	1	62,037
Ramapo College of New Jersey Mahwah, NJ	1	63,401
Rutgers The State Univ. Camden Camden, NJ	1	72,045
Seton Hall University South Orange, NJ	1	41,498
Smith College Northhampton, MA	1	88,280
Southern Illinois Univ. at Edwardsville Edwardsville, IL	2	122,544
Spelman College Atlanta, GA	1	69,735
St. John's University New York, NY	1	69,706
Swarthmore College Swarthmore, PA	1	56,598
Tuskegee University Tuskegee Institute, AL	1	58,721
University of Akron Akron, OH	3	209,783
University of Alabama in University University, AL	1	72,250
University of Alabama in Huntsville Huntsville, AL	1	67,122
University of Alaska Anchorage Anchorage, AK	1	70,240
University of Colorado at Denver Denver, CO	1	56,743

University of Kansas College of Health Sciences & Hospital School of Nursing and School of Allied Health Kansas City, KS	2	131,856
University of Maine Orono Orono, ME	1	71,197
University of Nevada Las Vegas Las Vegas, NV	1	71,018
University of Richmond Richmond VA	1	53,701
University of Texas Arlington Arlington, TX	1	67,659
University of Texas El Paso El Paso TX	1	50,800
University of Wisconsin Eau Claire, WI	2	136,677
Washburn University Topeka, KS	1	63,500
Wichita State University Wichita, KS	1	62,487
TOTAL	75	4,997,327

Mr. Conte. How many will you make with the additional $5 million in 86, assuming no rescission?

Dr. Raub. We anticipate that another 75 AREA grants will be awarded in FY 1986.

Mr. Conte. These are, on average, 2 year awards, is that correct? (If so, level funding would permit new awards to be made again in FY 1987?)

Dr. Raub. Yes, AREA grants are generally awarded for a period of two years. These grants were all forward-funded, i.e., total costs of the awards were obligated at one time. Level funding, i.e., $5, million in FY 1987, would permit us to make another set of approximately 75 grants. The exact number of awards that can be made is always a function of the sizes of the individual grants which include both direct and indirect costs.

Mr. Conte. At what level is the Small Business Innovation Research Program now functioning? Has this program made any contribution to scientific research at NIH? How many grants are now at the second level of development, and do you see anything exciting coming out of these grants yet? For the record, please indicate the average size of the grants for Phase 1, and for Phase 2.

Dr. Raub. This year the SBIR Program set-aside, as mandated by P.L. 97-219, is pegged at 1.25% of the funding agency's extramural R&D budget. In NIH's case, this percentage translates to approximately $50.6 million, following reductions made in accordance with the Balanced and Emergency Deficit Control Act of 1985 and proposed rescissions to the FY 1986 budget.

There are currently 114 active Phase II grants. Since the first group of Phase II grants will not be completed until the end of FY 86, it is premature at this time to draw any definitive conclusions about the outcome of these projects. However, NIH is currently supporting several SBIR projects that appear to be promising. Several examples are as follows:

- The product being developed is a tunable dye laser with output characteristics that would make it particularly suitable for the treatment of skin lesions of various sorts and colors. To date, there has been excellent clinical and engineering progress, and the company expects to have its product on the market by 1987. At the present time, six units have been manufactured, five of which are in use at the cooperating clinical center, Harvard Medical School. However, the sixth unit has been sold to Northwestern University, thus qualifying as an indication which suggests movements towards pay-off in a marketable device.

- The product provides for improved automated monitoring of physiological parameters via implantable telemetry, computer-based data acquisition, and on-line data analysis techniques. This research will result in a variety of products for laboratory applications, including telemetry-based systems for monitoring, logging, and analyzing blood pressure, EKG, temperature, gross movement, and other low frequency physiological parameters.

- With support from an NIH SBIR grant, the principal investigator and associates are developing a diagnostic test to identify carriers of cystic fibrosis.

- The product under development is a non-invasive mechanical device that generates vibrations and sound for use in a baby's crib. Data generated in clinical studies show that the conditions developed significantly reduce colic in infants.

- The grantee has developed a blood cell separator based on new ultrasonic techniques involving a method for aggregating and moving particles whose acoustic properties differ from those of the medium in which they are suspended. This method provides a controlled way of separating and moving blood cells from plasma.

FULL-TIME EQUIVALENTS

Mr. Conte. What was the FTE level in the Office of the Director in FY 1985, and what do you project, assuming no rescissions, for FY 1986, and under the President's budget for FY 1987?

Mr. Nicholas. The FTE level in FY 1985 was 539. Assuming no rescissions, the levels for FY 1986 and FY 1987 will be approximately 519.

Mr. Conte. For the record, would you provide the FTE levels in the Office of the Director and for NIH as a whole for the last 10 years, up to and including the proposal for FY 1987, and if you would, give us your impression of what the decline in FTE's has meant for your operations in the Office of the Director and for NIH as a whole.

Mr. Nicholas. The full-time equivalent (FTE) system for counting personnel has only been in effect at NIH since 1981. FTEs for 1981-1987 are as follows:

	Actual					Estimate	
	FY81	FY82	FY83	FY84	FY85	FY86	FY87
Office of Director	540	556	563	559	539	519	519
Total NIH	12,637	12,689	13,414	13,661	13,100	12,649	12,649

The NIH has been under various hiring freezes since FY 1985 in order to achieve its FTE ceilings. In addition to hiring freezes, efforts have been made to contract out, and NIH is looking at ways to improve productivity, such as organizational restructuring and improvements in efficiency. The Office of the Director has been part of some of these efforts.

MOTOR VEHICLES

Mr. Conte. I see that your budget request for FY 1987 is for 6 cars, as compared with 10 cars in FY 1986. Who gets to use cars at NIH, and how many do you have altogether?

Dr. Becker. Government cars are assigned to a central motor pool at the NIH and are used by employees engaged in official business. This includes travel between government office buildings, transportation of patients, pick-up and delivery of research materials, travel to and from area airports, etc. Presently, the fleet has fifty-five cars available for use by NIH employees. These vehicles are replaced according to schedules issued by GSA based on age and mileage.

TRAVEL

Mr. Conte. What's the travel budget in the Office of the Director, and for NIH as a whole?

Mr. Nicholas. The FY 1987 travel budget for the Office of the Director is $173,000 and $13,062,000 for NIH as a whole.

Mr. Conte. Do you have any idea how much of the grant money awarded by the NIH is used to support travel?

Mr. Nicholas. NIH awarded approximately $39 million dollars in support of travel for scientific purposes on all research mechanisms during FY 85. This was approximately 2% of the total direct costs awarded in support of these mechanisms.

FUNDING IN FY 1987 AT FY 1986 APPROPRIATION LEVEL

Mr. Conte. As my wrap-up question on the NIH, what would be the impact on NIH if we provided a freeze level of funding in FY 1987 at the FY 1986 pre-sequestration level?

Dr. Wyngaarden. If Congress provided the same level for FY 1987 as the FY 1986 appropriation (pre-sequestration) of $5,360.4 million, AIDS funding excluded, the increase of $424.2 million would be used as follows:

	(in millions)
FY 1987 Budget Request	$4,936.2
Noncompeting research projects grants - The additional funds would provide support for 549 additional awards resulting from the funding of 6,073 competing research projects in FY 1986 in lieu of 5,492 reflected in the FY 1986 revised estimate. In addition, this increment would also provide an increase in the average cost of an award.	169.3
Competing research project grants - The additional funds would provide support for 5,500 competing awards in FY 1987, an increase of 396 grants over the request, and provide for an increase in the average cost of an award.	94.5
Research centers - The additional funds would provide for the restoration of the 11 research centers reduced in the FY 1987 request and a small increase in average costs.	18.0
Small instrumentation program - The funds would provide modest support to begin to address the need for small instrumentation (equipment costing between $5,000 and $60,000).	12.0
Extramural animal facilities - The additional funds would provide for expansion of the extramural animal facilities renovation program.	3.0
Research career programs - The additional funds would provide for approximately 55 awards.	3.0
Research training - The additional funds would provide for 9,860 trainees, an increase of approximately 600 over the FY 1987 request.	13.0
R&D contracts - The additional funds would provide a current services level for research and development contracts.	15.0
Clinical trials - The additional funds would provide for the initiation of several major new clinical trials.	15.5

Intramural research - The additional funds would provide for administrative cost increases and for modest program expansion.	37.0
Research management and support - The additional funds would provide for administrative cost increases.	4.0
Cancer control - The additional funds would provide for increased prevention activities.	2.0
Extramural construction - The funds would provide support for needed renovation of extramural research facilities.	5.0
National Library of Medicine - The additional funds would provide for the current services level and a small program increase.	2.0
Office of the Director - The additional funds would provide $9.0 million for the small and minority universities and colleges program and $1.0 million for administrative cost increases.	10.0
Buildings and Facilities - The additional funds would provide an increase of $10.0 million for the upgrading of the NIH intramural animal facilities; $5.0 million for the 9th year of the 15 year project of the Clinical Center modernization program; $4.4 million for the planning of the Child Health/Neurosciences building; and $1.5 million for design of facilities to replace currently leased research facilities at the National Institute of Environmental Health Sciences.	20.9
FY 1987 Revised	$5,360.4

AREA/RMCI

Mr. Stokes. Yesterday, I asked Dr. Pickett, a number of questions pertaining to the Research Centers in Minority Institutions Program. Since the funding for this program is part of the Office of the Director, I would like to know who made the recommendation that $9 million in FY 1986 funding for the RCMI and the AREA initiatives be rescinded? Do you agree with this proposal? What are you plans for the RCMI and the AREA initiatives in FY 1987?

S-1

Dr. Raub. A rescission of approximately $9.1 million is proposed from the small and minority universities and colleges program. The Congress provided $20.0 million for this program in the FY 1986 appropriation, an increase of $10.0 million over both the FY 1985 funding level and the FY 1986 request. Given the need to reduce Federal expenditures because of the growing deficit, the Administration believed that such a significant add-on was unnecessary for a new program begun in FY 1985 with an initial appropriation of $10.0 million. We plan to continue this program in FY 1987 at the FY 1985 level of $10.0 million.

Mr. Stokes. FY 1985 was the first year of operation for the AREA awards. Can you tell us generally how this program is working?

-2

Dr. Raub. We believe that our first year has been very successful. The number as well as the quality of applications has made the AREA Program very competitive. Of the 423 applications submitted, 343 were recommended for approval and 75 were funded.

Mr. Stokes. As you know, the purpose of the AREA awards is to provide research opportunities for scientists at institutions that have not previously received significant amounts of NIH support. How did you carry out this directive?

Dr. Raub. The AREA Program guidelines were disseminated to a large number of institutions that were within that universe of "smaller, less prominent, four-year, public and private colleges and universities which provide undergraduate training for a significant number of our nation's research scientists but which have not shared adequately in the growth of the NIH extramural program." Furthermore, announcements were placed in the chronicle of Higher Education, Science, the Federal Register and the NIH Guide to Grants and Contracts as well as in the newsletters of 16 associations representing educational institutions that would be eligible for AREA grants. Considerable effort was made to reach the "target" population for which the AREA Program was intended.
Of the 58 institutions awarded AREA grants, 32 have received $1 million or less of research support from NIH over the last 24 years. Nine of these have never been awarded any research grants or contracts by NIH in the past.

Mr. Stokes. How many awards were made in 1985 and what was the average amount of the award?

Dr. Raub. 75 AREA grants were awarded from the FY 85 appropriation of $5 million. The cost of the average award was approximately $66,600. These grants were all forward-funded, i.e., total costs of the awards were obligated at one time.

Mr. Stokes. How many AREA awards were made in 1985 to historically black colleges?

Dr. Raub. In FY 1985 three AREA grants were made to historically black colleges/universities: Benedict College (Columbia, South Carolina), Spelman College (Atlanta, Georgia) and Tuskegee University (Tuskegee, Alabama).

Mr. Stokes. For the record, please supply a list of all institutions receiving AREA awards, the amounts received and also indicate how much each institution has received in previous NIH funding.

Dr. Raub. The following provides the names of those institutions that were awarded AREA grants, the number and dollar amount of these grants and the number and dollar amount of research awards received from NIH since 1962 (the year in which NIH research application/award data was converted into an easily accessible, computerized data base).

ACADEMIC RESEARCH ENHANCEMENT AWARDS

Institution	Area Award		Other Awards	
City and State	No.	Amount	No.	Amount
American University Washington, DC	1	60,404	67	2,901,400
Auburn University at Auburn Auburn, AL	1	59,332	161	4,838,933
Ball State University Muncie, IN	4	252,997	22	740,788
Barnard College New York, NY	1	85,299	27	901,426
Benedict College Columbia, SC	1	66,991	28	3,097,034
Bennington College Bennington, VT	1	59,088	7	54,125
Bryn Mawr College Bryn, PA	2	153,591	87	2,623,920

California State Polytech University Pomona, CA	1	63,572	3	156,015
California State Univer. at Long Beach Long Beach, CA	2	130,224	63	1,852,951
California State Univer. at Northridge Northridge, CA	2	128,611	72	2,561,713
California State Univer. at Fullerton Fullerton, CA	1	61,735	41	1,302,314
Carleton College Northfield, MN	1	77,413	2	10,434
Clark University Worcester, MA	2	146,677	155	4,739,159
Clemson University Clemson, SC	2	149,338	168	5,387,426
Colgate University Hamilton, NY	1	53,350	4	146,688
New York State College at Old Westbury Old Westbury, NY	1	56,459	16	2,287,585
College of Charleston Charleston, SC	1	81,926	--	---
New York State College College of Techonlogy Utica-Rome Utica, NY	1	63,500	--	---
Duquesne Univeristy Pittsburgh, PA	1	78,538	99	2,346,095
Eastern Michigan Univ. Ypsilanti, MI	1	63,608	1	47,561
Franklin and Marshall College Lancaster, PA	1	64,649	27	786,930
Haverford College Haverford, PA	1	59,035	144	4,548,684
Kenyon College Gambier, OH	2	144,489	17	236,426
Lamar Univeristy Beaumont, TX	1	51,808	--	---

Louisiana State Univ. Univ. of New Orleans New Orleans, LA	1	67,860	83	2,781,371
Luther College Decorah, IA	1	63,495	--	---
Manhattan College Bronx, NY	2	140,581	34	1,054,132
Memphis State Univer. Memphis, TN	1	71,500	27	1,851,952
Miami Univer. Oxford Oxford, OH	2	126,207	55	1,269,465
Mount Holyoke College South Hadley, MA	3	219,409	80	2,009,582
Murray State Univer. Murray, KY	1	61,096	5	98,899
Northern Kentucky Univ. Highland Heights, KY	1	79,451	--	---
Phillips University Enid, OK	1	63,496	--	---
Radford University Radford, VA	1	62,037	--	---
Ramapo College of New Jersey Manwah, NJ	1	63,401	--	---
Rutgers The State Univ. Camden Camden, NJ	1	72,045	2	37,214
Seton Hall University South Orange, NJ	1	41,498	37	559,795
Smith College Northhampton, MA	1	88,280	69	1,914,149
Southern Illinois Univ. at Edwardsville Edwardsville, IL	2	122,544	69	2,115,992
Spelman College Atlanta, GA	1	69,735	3	244,886
St. John's University New York, NY	1	69,706	47	1,245,408
Swarthmore College Swarthmore, PA	1	56,598	10	439,736

Tuskegee University Tuskegee Institute, AL	1	58,721	155	10,007,078
University of Akron Akron, OH	3	209,783	46	1,499,958
University of Alabama in University University, AL	1	72,250	157	5,884,072
University of Alabama in Huntsville Huntsville, AL	1	67,122	10	468,399
University of Alaska Anchorage Anchorage, AK	1	70,240	6	608,582
University of Colorado at Denver Denver, CO	1	56,743	5	201,328
University of Kansas College of Health Sciences & Hospital School of Nursing and School of Allied Health Kansas City, KS	2	131,856	2	76,919
University of Maine Orono Orono, ME	1	71,197	150	4,452,399
University of Nevada Las Vegas Las Vegas, NV	1	71,018	3	122,946
University of Richmond Richmond VA	1	53,701	4	640,934
University of Texas Arlington Arlington, TX	1	67,659	24	1,123,049
University of Texas El Paso El Paso TX	1	50,800	26	3,778,350
University of Wisconsin Eau Claire, WI	2	136,677	11	653,602
Washburn University Topeka, KS	1	63,500	16	90,921
Wichita State University Wichita, KS	1	62,487	34	750,626
TOTAL	75	4,991,327	[illegible],411	87,559,351

EQUAL OPPORTUNITY

Mr. Stokes. It is my understanding that nearly all the Bureaus, Institutes, and Divisions at NIH have an Equal Employment Officer, but that these persons do not report to the Director of Equal Opportunity for NIH. Do you believe that the Director of the Division of Equal Opportunity has adequate authority and resources to effectively implement strong EEO policies at NIH? Why?

Mr. Nicholas. As is consistent with all management components within the Office of the Director (OD), NIH, in their relationship to the Bureaus, Institutes, and Divisions (BIDs), the Division of Equal Opportunity (DEO) provides overall leadership and guidance to the BIDs on all phases of equal opportunity. Although BID EEO Officers report to their respective BID director, as do all BID components, liaison is maintained with the Director, DEO and DEO staff for consultation and assistance regarding problems and progress of equal employment opportunity programs in their respective organizations. The DEO has the same mechanisms available to it for program implementation as do the other central functions located within the Office of the Director.

The need for additional resources has not been a barrier to the effective implementation of strong EEO policies at NIH.

Mr. Stokes. It is my understanding that the NIH Equal Opportunity Advisory Council has been or will be abolished, to be replaced by an NIH Advisory Committee of Equal Opportunity. Is that correct?

Mr. Nicholas. It has been proposed that the NIH Advisory Council be restructured and that the name be changed to NIH Advisory Committee for Equal Opportunity. Final action has not been taken on the proposal.

Mr. Stokes. What is the rationale for the restructuring of this committee?

Mr. Nicholas. The proposal to restructure the NIH EEO Advisory Council resulted from a review by the Director, DEO, as requested, of the many NIH organizations functioning as advisory councils, committees and as special interest groups (SIGs). Reviewed were their structure, mission, and results of their efforts in effecting changes. In summary, the several organizations were found to have had formal and informal mandates to monitor, facilitate and evaluate management actions related to equal employment and civil rights responsibilities at NIH. Their primary efforts have been directed toward correcting imbalances in employment, and the results of their efforts vary from not being easily determined to being explicit and clearly identifiable. Finally, it was evident that the groups have functioned separately, with no apparent coordination of goals or program actions.

Based upon the above and the realization of: 1) the NIH EEO program requirements; 2) the prospect of budget cuts and its impact upon resources; and 3) the need to increase productive EO program efforts through collaboration, cooperation and integration of group efforts, the Director, DEO proposed changes in structure, function, roles, relationships, responsibilities, and direction of the NIH EEO Advisory Council, committees and SIGs. The proposed changes are designed to:

- Institute total program approach to review, analysis and monitoring functions;
- Relate restructured group goals and objectives to NIH EO goals and objectives;
- Identify specific activities/initiatives, plan and assign actions and evaluate results;
- Integrate restructured group initiatives, plans and actions;
- Promote collaboration and cooperation among groups through committee assignments/activities;
- Establish team approach to restructured groups' function;
- Integrate and focus the advisory groups' functions;
- Develop total program awareness within the restructured groups;
- Establish approach to responding to crisis situations or unanticipated requirements.

It should also be noted that, following a review of the NIH Advisory Council mission and an evaluation of its activities, the members of the Council recommended to the Director, DEO, that a change in structure be made. The proposal for restructuring presented by the Director, DEO, was reviewed by the BID EEO Officers and was endorsed by them for implementation.

Mr. Stokes. My understanding is that the new committee will be comprised of 43 persons and will meet only once a year. Is that correct?

Mr. Nicholas. The Advisory Committee for Equal Opportunity will consist of an executive planning group and six (6) subcommittees (43 members). The full Advisory Committee of 43 members will meet annually, or as required to address special concerns, for orientation and presentation of subcommittee annual reports. The Executive Planning Group will meet semiannually with the subcommittee chairs for planning, evaluation and reporting. Subcommittees will meet monthly, or at the direction of the Executive Planning Group.

Mr. Stokes. How will this arrangement be more effective than the old one?

Mr. Nicholas. The proposed restructuring would be more effective in operation and effect as a result of its mission, function and membership.

The Advisory Committee's mission would be to:

- Submit recommendations to the Director, DEO, annually, for developing NIH equal employment opportunity and civil rights activities, goals and objectives;

- Surface issues related to NIH EEO civil rights activities at the agency and/or BID level;
- Establish and maintain an integrated NIH effort on equal opportunity and civil rights activities; and

- Assess program allocations and distribution of resources agency wide, vis a vis EEO and civil rights requirements and related program goals.

The Advisory Committee's function would be to focus on agency wide issues, projects and activities through the six (6) subcommittees that will address the areas of:

- Employment (recruitment, selection hiring promotions, appraisals, training, disciplinary actions, and termination);

- Special Emphasis Programs (FWP, HEP, Handicapped, Asian/Pacific Islander, Native American Indian, and Black concerns);

- Discrimination complaints (counselors, complaints processing);

- Internal/External Activities (committees, boards, task forces, and special groups);

- Grants/Contracts and Extramural Programs; and

- Educational/Cultural Activities (Black, women, Hispanic, Asian/Pacific Islander, Native American Indian, and handicapped).

The Advisory Committee's membership and terms of appointment will be established to provide the broadest representation of NIH program and organizational responsibility.

Represented will be members from:

- The Office of the Director (DEO program management staff and OD administrative staff),

- Bureaus, Institutes, and Divisions (EEO Officers, Institute Directors, Scientific Directors, Executive Officers, Personnel Officers, Extramural Program Management Committee, Grants Management Advisory Committee, and Research Contracting Committee),

- Special Interest Groups (Women's Advisory Committee, Hispanic American Advisory Committee, Handicapped Employees Committee, Asian Pacific Islander Equal Opportunity Advisory Committee, and Native American Indian Committee).

Mr. Stokes. The March 1986 report of the General Accounting Office on Affirmative Action and Equal Opportunity at NIH found that NIH took longer to render decisions and resolve discrimination complaints after receiving investigation reports from the Department of Health and Human Services than any other component of the Public Health Service, and the median time increased from 230 days to nearly 400 days. Why does it take so long to process discrimination complaints at NIH?

Mr. Nicholas. Problems associated with the length of time taken to process complaints of discrimination between FYs 1982 and 1984 resulted from the lack of an experienced manager within the complaints branch in the NIH Division of Equal Opportunity; the long-standing practice of contracting out the preparation of complaints of discrimination, which resulted in limited controls on the quality of reports, requiring extensive revisions by the NIH; and inadequate staff resources in the NIH DEO. These problems were remedied during FYs 1984 and 1985, as noted in the GAO report.

Mr. Stokes. The GAO report cites the loss of key experienced staff, staff who lack the skills to manage the work, and personality conflicts among staff are major factors contributing to long complaint processing times. What are you doing to remedy these problems?

Mr. Nicholas. The NIH, during FY 1984 and 1985 took several actions to improve the timeliness of processing complaints of discrimination. The Director, Division of Equal Opportunity, hired in January 1984:

- Appointed a new manager of the division's complaints branch.
- Discontinued contracting to have disposition reports prepared.
- Employed a private consultant to train division staff in preparing disposition reports.
- Hired additional support staff.
- Held regular meetings with EEO officers representing the various NIH Bureaus, Institutes, and Divisions.

These activities resulted in the issuance of 41 proposed dispositions between December 1984 and August 1985 and the elimination of the backlogged cases over which the division had control. In addition, the processing time for complaints has dropped from the 395.5 days in FY 1984 to 137 days in FY 1986. The elimination of the backlog and improved processing time has allowed staff to process complaints in the established DHHS timeframes, and time to address other areas involved with complaints processing, i.e., providing appropriate BID staff with relevant information concerning complaints in their BIDs. The aforementioned actions have also reduced to a minimum personality conflicts among staff.

Mr. Stokes. How many people in the Division of Equal Opportunity handle discrimination complaints?

Mr Nicholas. Four (4) professionals and one (1) clerical. The branch has one vacant clerical position which has not been filled due to the existing hiring freeze.

Mr. Stokes. Do you believe that this is an adequate number? Why?

Mr. Nicholas. The existing staff have been able to process the complaints filed against the NIH. The previously existing backlog has been eliminated and the processing time has been significantly reduced.

Mr. Stokes. The GAO found that NIH has not established hiring goals for minorities and women. What plans do you have to establish such goals?

Mr. Nicholas. The Director, NIH, has appointed a committee to develop methodology for establishing meaningful goals that will meet the EEOC requirements. Once goals are established, this committee will develop a mechanism for implementation of these goals in the NIH Bureaus, Institutes, and Divisions. To augment the committee's actions, the NIH Division of Equal Opportunity (DEO) has already investigated the use of automated systems for the calculation of goals and manipulation of data for meeting affirmative action requirements and has proceeded with preparing the documentation required to purchase the necessary computer hardware of software packages.

Mr. Stokes. The GAO also found that NIH minority and female recruiting plans have not been implemented in accordance with EEOC and OPM requirements. What steps do you plan to take to strengthen the implementation of minority and women recruiting strategies?

Mr. Nicholas. The NIH prepared minority and female recruiting plans in accordance with instructions and guidance received from the Department of Health and Human Services and the U.S. Public Health Service. Five (5) NIH components did not prepare minority and female recruiting plans. The Director, NIH will direct the five components that do not have minority and female recruitment plans to prepare and submit them to the NIH Division of Equal Opportunity (DEO).

Since the current AAP/FEORP planning cycle ends in FY 1986, and new plans will have to be prepared, the NIH will closely review and monitor the development and implementation of these plans in its component organizations.

Mr. Stokes. Minorities and women were underrepresented as of December 1984 in 63 of 108 race, ethnic origin, gender, occupation and grade level categories, according to the GAO. What steps do you plan to take to identify and eliminate employment barriers for minorities and women?

Mr. Nicholas. The NIH has conducted barrier analyses in accordance with the Public Health Services (PHS) guidance on AAP/FEORP. Analyses of four (4) series have been completed by NIH. Analyses of the remaining target series are underway, and it is anticipated that they will be completed before the end of Fiscal Year (FY) 1986. Should any barriers to equal employment opportunities be found, NIH will take appropriate actions to correct the situation.

It should be also noted that NIH participated in the development of the methodology for a PHS-wide study (nine months in duration) on barriers to the employment of Hispanics and Native Americans, conducted a barrier analysis in its (NIH) component organizations, and participated in analyzing data and writing the PHS final report issued in September 1984. Since that time, NIH has implemented several of the recommendations contained in the PHS report.

Mr. Stokes. Who in the Office of the Director has the responsibility for developing "barrier analyses" to identify possible impediments to meeting affirmative action goals -- the Division of Equal Opportunity or Division of Personnel?

Mr. Nicholas. The Division of Personnel Management (DPM) has responsibility for the conduct of barrier analyses. The Division of Equal Opportunity provides the DPM with data on the representation of minorities and women by occupation and grade level, consults with the DPM as they conduct the analyses, and reviews analyses once they are completed.

Mr. Stokes. The GAO report indicates that barrier analyses were conducted by the Division of Personnel Management for the chemist, medical officer and contract specialist occupational series from August to December 1985. Please insert copies of these Analyses for the record.

Mr. Nicholas. The following is provided in response to the request for copies of the three (3) barrier analyses reports prepared by the NIH Division of Personnel Management: (It should be noted that although the GAO report states that these three analyses were conducted between August and December 1985, the barrier analysis of the Chemist series was conducted in September 1982.)

Barrier Analysis: Chemists, GS-1320

1. Underrepresentation (see attached worksheet for complete data)

A comparison of the NIH work force of Chemists as of 6/26/82, indicated underrepresentation in the following categories, with servere[1] underrepresentation underlined. Summaries are also presented for males, females, nonminorities and minorities.

Entry Level (8 positions)	Underrep Index	Positions
Nonminority males	56.8	2.4
Black females	0.0	*
Hispanic males	0.0	*
Asian and PI males	0.0	*
Am. Ind. and AN males	0.0	*
Am. Ind. and AN females	0.0	*

Summary Data	All males	68.2	1.9
	All females	187.1	Overrepresented
	All nonminorities	68.4	2.3
	All minorities	432.0	Overrepresented

Mid Level (255 positions)		
Nonminority males	47.8	89.0
Hispanic males	0.0	5.6
Hispanic females	30.0	1.6
Am. Ind. and AN males	0.0	*
Am. Ind. and AN females	0.0	*

Summary Data	All males	55.1	83.8
	All females	223.1	Overrepresented
	All nonminorities	86.8	30.9
	All minorities	236.9	Overrepresented

Senior Level (287 positions)		
Nonminority females	56.9	30.1
Black males	22.8	6.8
Black females	0.0	6.4
Hispanic males	0.0	6.3
Hispanic females	35.0	2.9
Am. Ind. and AN males	0.0	*
Am. Ind. and AN females	0.0	*

Summary Data	All males	113.0	Overrepresented
	All females	65.1	26.7
	All nonminorities	97.0	8.0
	All minorities	132.0	Overrepresented

* = underrepresentation is less than one position

1/ Servere underrepresentation exists when the index is below 50.

Analysis of Data

Entry Level: Underrepresentation for specific minorities is not statistically significant due to the small number (8) of positions involved. The only underrepresentation requiring at least one full position is for nonminorities, and more specifically, nonminority males. Consequently, there is no basis for conducting further barrier analysis for this level.

Mid Level: Underrepresentation at this level is severe for nonminority males and Hispanics. Representation of all minorities exceeds professional clf data indicating that screening and selection of applicants do not constitute a barrier. The ratio of positions needed to achieve full representation (i.e., 89 non-minority males, 5.6 Hispanic males and 1.6 Hispanic females) seems more indicative of the labor force for Chemists. Barrier analysis should focus on recruitment efforts and the potential for developing the labor force to increase representation in these categories.

Senior Level: Underrepresentation at this level exists for virtually all categories except Asian and Pacific Islanders, who are highly overrepresented. As a result, minorities as a whole are overrepresented, while 30 positions are needed to correct underrepresentation for white females. This data suggests a need to determine the availability of qualified females and underrepresented minorities at this level.

2. Labor Market Assessment

Civilian labor force data are constant regardless of occupations or grade levels being considered. Consequently, even though underrepresentation for a given group may be assessed fairly using the clf, the indicated availability of a qualified work force may be inaccurate. Relevant labor market data are a more accurate reflection of work force availability. The following figures compare the percentage distributions of the NIH work force, the professional clf, and relevant labor market data for Chemists at the senior level.

	Female	Black	Asian	Hisp.	Total Minority
NIH	17.40	.70	10.40	.35	11.50
CLF	26.72	5.30	1.30	3.21	8.60
RLM	10.60	0.00	7.00	0.00	7.00

From this information it is evident that the actual availability of women and minorities other than Asians and Pacific Islanders for positions at the senior level is significantly less than is indicated be aggregated clf data, and constitutes a barrier to their full representation. Additionally, the actual availability of Asians and Pacific Islanders is greater than indicated by clf data (by a factor of five) to the detriment of other minorities. Finally, the distribution of the NIH work force reflects a pattern of selection that is favorable to all minority groups compared to their respective availability.

3. Objective

In order to achieve full representation of senior level Chemists in relation to the clf figures, it will be necessary for NIH to recruit and select at a rate in excess of current labor market availability. As already indicated, the available outside female and minority labor force having the requirements for employment at the senior level is limited and highly sought. However, since NIH primarily selects senior level scientists through conversion from its Staff Fellowship Programs, this would be the most fruitful method for effecting change. Staff fellows are recruited from recent graduates at the doctorate level who show promise as researchers, but who lack the experience necessary to qualify for appointment at the senior level. They are awarded excepted appointments for limited periods of time and are provided post doctorate experience in a structured research environment. Later, having developed basic eligibility for the senior level, they may be considered for permanent appointments.

Through more aggressive recruiting of minority and female candidates for the NIH Staff Fellowship Program, NIH could expand the potential labor market for females and minorities, and heighten its appeal for target groups through faculty and other school contacts. This approach shows the greatest potential for helping correct the underrepresentation of senior level minority and female chemists. This same strategy would generally pertain to other intramural disciplines.

SELECTIVE VARIABLE — NATIONAL INSTITUTES OF HEALTH
Type of appointment: Full-time & Part-time Permanent — UNDERREPRESENTATION [illegible] INDEX
Employment Category: Professional

Occupation: Chemist (1320)

POPULATION	ENTRY LEVEL Work Force #	%	Labor Force %	Underrepres. Index *	MID LEVEL Work Force #	%	Labor Force %	Underrepres. Index *	SENIOR LEVEL Work Force #	%	Labor Force %	Underrepres. Index *
Non-minority Males	1	12.5	66.88	18.7	82	32.16	66.88	48.1	214	74.6	66.88	N/A
Non-minority Females	4	50.0	24.44	N/A	120	47.06	24.44	N/A	34	11.9	24.44	56.9 30.0
Black Males	1	12.5	3.07	N/A	16	6.27	3.07	N/A	2	.7	3.07	22.8 6.0
Black Females	0	0.0	2.21	0.0 *	11	4.31	2.21	N/A	0	0.0	2.21	0.0 6.0
Hispanic Males	0	0.0	2.21	0.0 *	0	0.0	2.21	0.0 5.6	0	0.0	2.21	0.0 6.0
Hispanic Females	1	12.5	1.00	N/A	1	.39	1.00	39.0 1.6	1	.35	1.00	35.0 2.0
Asian/PI Males	0	0.0	1.01	0.0 *	5	1.96	1.01	N/A	21	7.3	1.01	N/A
Asian/PI Females	1	12.5	.29	N/A	20	7.84	.29	N/A	9	3.1	.29	N/A
Am. Ind./Al Males	0	0.0	.11	0.0 *	0	0.0	.11	0.0 *	0	0.0	.11	0.0 *
Am. Ind./Al Females	0	0.0	.04	0.0 *	0	0.0	.04	0.0 *	0	0.0	.04	0.0
TOTAL EMPLOYEES	8	100%	X X	X X	255	100%	X X	X X	287	100%	X X	X X
Non-min	5	62.5	91.12	68.4 [illegible]	202	79.26	91.12	86.8 (30.9)	254	88.5	91.32	97.0
Min	3	37.5	8.68	432.0 (over)	51	20.74	8.68	238.9 (over)	33	11.5	8.68	132.0 (over)

*Underrepresentation Index Formula:

Workforce % / Labor Force % x 100 URI

Entry Level includes the following grades: GS-5, 7

Labor Force Source:
National Professional
1 position = 12.5% (indicates limited opportunity for positions)

Mid Level includes the following grades: GS-9, 11, 12

Labor Force Source:
National Professional
1 position = .39%

Note: * = Underrepresentation is less than one position

Senior Level includes the following grades: GS-13, 14, 15
GM-13, 14, 15
SES/SSS

Labor Force Source:
National Professional
1 position = .35%

Barrier Analysis: GS-602 Medical Officer

1. Analysis of recruitment sources used to attract qualified or qualifiable applicants to fill identified targeted occupations:

   a. Recruitment resources used to attract GS-602:
      (1) Medical Staff Fellowship Program.
      (2) MARC and MBS for undergraduate exposure.
      (3) Summer Research Fellowship Program.
      (4) Send letters to Deans of Student Affairs at Medical Schools and Deans of Minority Affairs.
      (5) Cooperate with the National Association of Minority Medical Educators and Student National Medical Associations.
      (6) Visits to various medical schools.
      (7) Advertise in medical school newsletters and Health Careers Network Newsletter.

   b. Ranking of recruitment resources by effectiveness:
      (1) Visits to medical schools and presentation of NIH information on research programs.
      (2) Contact with minority affairs directors.
      (3) Visits with minority student associations.

2. Analysis of Selection Process Under the Uniform Guidelines on Employee Selection Procedures (UGESP)

   The UGESP and Equal Employment Opportunity Commission (EEOC) Federal Affirmative Action Instructions, MD-702, dated December 11, 1979, require each agency to examine the employee selection process for each job to determine adverse impact on employment opportunities of members of a race, national origin, or sex group. Adverse impact as defined in FPM Letter 300-25, Section 16B of the UGESP, is a substantially different rate of selection, hiring, promotion, or other employment decisions which work to the disadvantage of members of a race, sex, or national origin group.

   In our attempt to examine the NIH selection process we asked BID Personnel Officers and EEO Officers the following questions:

   a. Are selecting officials provided with technical assistance in the development of selection critieria so as not to exclude the employment of the target population?
   b. Are steps taken to ensure that there are no unrealistic experience or educational requirements for positions?
   c. Do personnel staff review the rating criteria submitted by selecting officials to ensure that there are no barriers that could impede the employment of the target population?
   d. Are personnel staff and/or selecting officials knowledgeable concerning alternative mechanisms for filling vacancies, e.g., restructuring, special hiring authorities, etc.?
   e. Are steps taken to ensure that agency qualification review boards include minority and EEO staff representation?

All of our questions received affirmative responses. In one BID we found a criteria evaluation committee developing selection criteria and providing technical assistance to selecting officials.

Being mindful of all the positive responses we found it necessary to continue and ask BIDs to describe and barriers that they might see in the selection process that has impeded the selection of the target population. Most BIDs said "none." But some suggested the following:

a. Racial, sexual and peer prejudicies of selecting officials.
b. Selecting officials tend to favor the same educational institutions and tend to screen out applicants based on what college or university they attended.
c. Selecting officials are unwilling to accept delays associated with extensive recruiting efforts.

Anticipating the above responses we also asked "Are supervisors and managers made aware of their BID's work force EEO profiles?" All said yes. Then we asked "Are steps taken to increase selecting officials sensitivity and awareness of the severe underrepresentation of the target population?" Seventy-four percent of the BIDs said they accomplished this by distribution of information or by EEO and personnel staff discussions with selecting officials. The remaining 26 percent indicated that they are beginning to initiate steps that will improve the awareness of selecting officials. While we were unable to find any adverse impact in the selection process under UGESP, some of the BIDs were able to remind us of subtle covert biases such as "what school an appliant graduated from." Time, understanding, sensitivity, and more time will probably do well to eliminate these intangibles.

3. Analysis of Promotion and Hiring Trends for each Underrepresented Group

An underrepresentation index URI of 100 equals parity in the charts. These figures are comparing FY 1983 statistics with FY 1984. (See Chart A)

Entry Level: N/A

Mid Level:

There was no change in the representation of minority males and females (URI = 0)

Senior Level

Nonminority females decreased from an URI of 88 to an URI of 85. Black females increased from an URI of 31 to an URI of 58. There was no change in the representation of Black males (URI = 0), American Indian males and females (URI = 0), and Hispanic females (URI = 0). Hispanic males increased from an URI of 32 to an URI of 59.

GS-602 Accessions for FY 1984 (See Chart B)

Analysis:

There were 21 accessions for FY 1984, i.e., 17 males and 4 females. Eleven were full-time permanent. Seven were full-time temporary, and three were part-time temporary. None was minority.

Department of Education data tells us that in 1981 approximately 12 percent (1833) of the graduates with degrees in medicine were minorities. The overall number of minorities graduating in medicine was increasing for the three previous years; however, this was just the contrary for Blacks during the same period.

4. Recommendations

In order for NIH to achieve URI parity for the GS-602 series positions, more aggressive affirmative recruiting will have to occur. At the undergraduate levels the MARC and MBS programs are invaluable resources for exposing college students to careers in the biomedical sciences. The Summer Research Fellowship Program could prove to be valuable recruiting tool. However, the Medical Staff Fellowship Program appears to show most promise as the best source for achieving parity.

Medical Staff Fellows are of the highest quality and scholastic achievement and they are assigned to senior investigators for two or three years to train in the biomedical sciences. Upon completion of their tour of duty they are eligible for consideration for conversion to a career position. This makes the Minority Medical Staff Fellow an excellent prospect for melting into the career work force and thereupon helping to improve the underrepresentation index for the target population.

These programs are fine, but to incure that they are always working a system of program review should be established for the conversion of minority medical staff fellows. For example, the current review committee, chaired by the Associate Director for Medical Education, Clinical Center, could be utilized for monitoring the conversion of minority medical staff fellows. This same committee, if expanded, could assist in the affirmative recruiting program of the agency.

CHART A

[illegible]
[illegible]

[illegible]

[illegible] 602- MEDICAL OFFICER

[illegible]	Non-Minor Males	Non-Minor Females	Black Males	Black Females	Hispanic Males	Hispanic Females	Asian/PI Males	Asian/PI Females	Am. Ind. Males	Am. Ind. Females
[illegible]										
Entry Level	N/A →									
Mid Level	75	100+	0	0	0	0	0	0	0	0
Senior Level	100+	85	0	58	59	0	100+	100+	0	0
[illegible]										
Entry Level	N/A →									
Mid Level	0	100+	0	0	0	0	0	0	0	0
Senior Level	100+	88	0	31	32	0	100+	100+	0	0
[illegible]										
Entry Level	N/A									
Mid Level	+75	0	0	0	0	0	0	0	0	0
Senior Level	0	-3	0	27	27	0	0	0	0	0

CHART B

[illegible] ACCESSIONS FOR FY [illegible]

[illegible]	Total		Black		Hispanic		American Indian		Asian		White	
	M	F	M	F	M	F	M	F	M	F	M	F
FTP	[illegible]	1	0	0	0	[illegible]	[illegible]	0	0	0	10	1
FTT	[illegible]	1	0	0	0	0	[illegible]	0	0	0	[illegible]	1
PTP	[illegible]	0	0	0	0	[illegible]	[illegible]	0	0	0	0	[illegible]
PTT	[illegible]	2	0	0	0	[illegible]	0	0	0	0	1	2
[illegible]	[illegible]	[illegible]	0	0	0	0	[illegible]	0	0	0	17	[illegible]

[illegible] denotes the following:

FTP Full time permanent
FTT Full time temporary
PTP Part time permanent
PTT Part time temporary

Barrier Analysis: GS-1102 Contract Specialist

1. Analysis of Recruitment Processes Used in Filling Targeted Occupations

   a. Recruitment resources used to attract GS-1102:
      (1) NIH Vacancy Announcements.
      (2) Applicant Supply File.
      (3) Cooperative Education Program.
      (4) Outreach Program.
      (5) College Career Fairs and Job Fairs.

   b. The NIH does not have a system to determine the number of women and minority group members who have applied for GS-1102 positions, or any other positions. Individual Bureaus, Institutes and Divisions (BIDs) may maintain this kind of information.

   c. Ranking of recruitment resources by effectiveness:
      (1) Applicant Supply File.
      (2) NIH Vacancy Announcements.

2. Analysis of Selection Process Under the Uniform Guidelines on Employee Selection Procedures

   The Personnel Officers and Equal Employment Officers of BIDs that hire Contract Specialists were contacted to determine (a) their involvement with selection criteria that does not impede the employment of the target population by using unrealistic experience or education requirements and (b) their involvement with representation on qualification review boards.

   We found that Personnel and Equal Employment Officers and their staffs are very involved in the employment selection process, including the review of all selection criteria and making recommendations to selecting officials on appropriate criteria and the adequacy of rating plans.

3. Analysis of Promotion and Hiring Trends for Each Under-represented Group

   An underrepresentation index (URI) of 100 equals parity in the charts. These figures are comparing FY 1982 statistics with FY 1984. (See Chart A)

   Entry Level

   Black males advanced from a URI of 69 to full representation. Asian females regressed from full representation to a URI of 0. There was no change in the representation of Hispanic males and females, Asian males, and American Indian males and females (URI = 0).

   Mid Level

   Black males decreased from a URI of 84 to a URI of 74. Black females advanced from a URI of 87 to full representation. Hispanic males regressed from a URI of 20 to a URI of 0. There was no change in the representation of Hispanic females, Asian males, and American Indian males and females (URI = 0).

Senior Level

Nonminority females increased from a URI of 43 to a URI of 58. Black females regressed from full representation to a URI of 69. There was no change in the representation of Hispanic, Asian, and American Indian males and females (URI = 0).

GS-1102 Accessions and Promotions for FY 1984 (See Chart B)

Analysis:

There were 6 accessions for FY 1984, i.e., 3 males and 3 females. Four were full-time permanent and 2 were part-time temporary. One was Black female.

There were 33 promotions for FY 1984, i.e., 4 males and 29 females. Thirty-one were full-time permanent and 2 were part-time permanent. Five or 15 percent were minorities, all Black females.

4. Results of Barrier Analysis Study

We could not find any adverse impact in the overall selection process for filling targeted positions.

Recruitment for FY 1984 was little to none, because of very few employment opportunities. In fact, for the past two fiscal years there was only one accession at the entry, GS-5-7, grade level. As a result of the lack of employment opportunities, there were no extensive outreach and external recruitment efforts.

Therefore, we did find the lack of an overall Outreach Program that would reach Hispanic and American Indian applicants for administrative positions. When one of these few vacancies occurred the selecting officials were unwilling to accept delays associated with extensive recruitment efforts. However, there are some suggested remedies to this problem as noted in the recommendations below.

We also found that the Career Opportunity Training Agreement (COTA) was the most dependable mechanism for bridging positions. The COTA works very well in an organization that does not have the routine transitional jobs, such as procurement clerk and procurement agent.

Recommendations

In order for NIH to achieve URI parity for the GS-1102 positions, certain training and employment opportunities will have to occur, such as:

a. Establishment of more bridge positions with career pathways designated.

b. Establihsment of more trainee positions using the Career Opportunity Training Agreement.

c. Development of an Outreach Program that will gather qualified applications for storage in the Applicant Supply File and future use when vacancies occur with a short advertising period.

d. Development of an Outreach Program that uses COOP students as its chief mechanism for filling targeted positions.

e. Development of an in-house crossover training agreement that will permit BIDs with mostly higher graded positions to interact with BIDs that have mostly lower graded positions thereby producing an exchange of research and development experiences that can be used agency-wide.

CHART A

FY 82-84 ACCOMPLISHMENT REPORT
PARITY/REPRESENTATION INDEX

Category ADMINISTRATIVE

Targeted Occupation 1102 - CONTRACT/PROC. SPECIALIST

Occupational Level	Non-Minor Males	Non-Minor Females	Black Males	Black Females	Hispanic Males	Hispanic Females	Asian/PI Males	Asian/PI Females	Am. Ind. Males	Am. Ind. Females
PR as of 6/84										
Entry Level	11	100+	100+	100+	0	0	0	0	0	0
Mid Level	61	100+	74	100+	0	0	0	100+	0	0
Senior Level	100+	58	100+	69	0	0	0	0	0	0
PR as of 6/82										
Entry Level	11	100+	69	100+	0	0	0	100+	0	0
Mid Level	75	100+	83	83	70	0	0	100+	0	0
Senior Level	100+	43	100+	100+	0	0	0	C	0	0
Net Change										
Entry Level	0	0	+31	0	0	0	0	-100	0	0
Mid Level	-14	0	-11	+17	-70	0	0	0	0	0
Senior Level	0	+15	0	-31	0	0	0	0	0	0

CHART B

GS-1102 ACCESSIONS FOR FY 90

	Total		Black		Hispanic		Amer-ican Indian		Asian		White	
Series 1102	M	F	M	F	M	F	M	F	M	F	M	F
FTP	2	2	0	1	0	0	0	0	0	0	2	1
FTT	0	0	0	0	0	0	0	0	0	0	0	0
PTP	0	0	0	0	0	0	0	0	0	0	0	0
PTT	1	1	0		0	0	0	0	0	0	1	1
Grand Total	3	3	0	1	0	0	0	0	0	0	3	2

Acronyms denote the following:

FTP Full time permanent
FTT Full time temporary
PTP Part time permanent
PTT Part time temporary

CHART B

[illegible]

Series 1102	Total		Black		Hispanic		American Indian		Asian		White	
	M	F	M	F	M	F	M	F	M	F	M	F
FTP	4	27	0	5	0	0	0	0	0	0	4	22
FTT	0	0	0	0	0	0	0	0	0	0	0	0
PTP	0	2	0	0	0	0	0	0	0	0	0	2
PTT	0	0	0	0	0	0	0	0	0	0	0	0
Grand Total	4	29	0	5	0	0	0	0	0	0	4	24

Acronyms denote the following:

FTP - Full time permanent
FTT - Full time temporary
PTP - Part time permanent
PTT - Part time temporary

CLINICAL CENTER

Mr. Early. Doctor, last year, I believe you indicated that all work on the Ambulatory Care Research Facility had been completed and that the ACRF was fully operational. Is the ACRF being used to the optimal level?

Dr. Wyngaarden. The Ambulatory Care Research Facility is really two buildings in one. The first, designed for research laboratories, is fully occupied and contributing daily to the health research program. The second, designed as clinic space for service of, and research on, patients is in full use but not exclusively for clinics. Nine floors are now clinics, and another is being changed from one type of clinic service to another. Another floor is being used for office swing space while regular space is under renovation in the original building.

Mr. Early. Do you feel the staffing level is sufficient to allow for optimum utilization -- or could greater use be made of the facility if you had more staff? If staffing is a problem, in what areas are there shortages?

Dr. Wyngaarden. Yes, we could make fuller use of the ACRF if additional staffing and funds were available. A good example is our inability to staff fully an Urgent Care Clinic, a service requested by the Ambulatory Care Committee of the Medical Board.

The biggest area of staffing shortage has been in nursing. A delicate balance exists between available beds, nursing, and other resources and the acuity and complexity of patient care and research demands. Clinical Center management is responsible for assuring that resources are adequately matched to patient care and research requirements. Patient care and research requirements vary dramatically with the nature of the diagnosis, treatment and protocol needs of patients. They vary with weekday, weekend and month of year fluctuations as well. The nursing resources available to care for patients are finite and quantifiable. Therefore, the numbers and kinds of patients tend to fluctuate and be adjusted to the available nursing staff. This means that, at any point in time, the unit may be 100% occupied by less acutely ill patients, whereas at another point it may be 50% occupied by very intensively and acutely ill patients who individually demand more nursing time. More predictable patient care requirements and more flexible nurse staffing arrangements would more adequately support a higher bed occupancy in the Clinical Center.

Mr. Early. What is the status of the Clinical Center renovation project? Are we on schedule? How much slippage has there been since the project started?

Dr. Becker. We are in the eighth year of the program. We now expect the program to run for a total of 15 years, rather than the 10 years envisioned in 1979 when the program began. The 5-year extension has been caused by the need to keep the clinical and laboratory research programs in the Clinical Center operational during construction. We found that disruptions to research and to the needs of patients were becoming unacceptable and decided last year on the 15-year schedule. In addition, we have had to initiate projects to accommodate technological advances that could not have been foreseen when the modernization effort began. These include the planned addition to surgery to meet current standards of air flow and space for high technology equipment in cardiac and neuro-surgery, and the construction of a facility with limited steel beams to permit the use of high field magnets in nuclear magnetic resonance (NMR) imaging and spectroscopy _in vivo_.

Mr. Early. Doctor, based on previous comments it would seem that greater use could be made of the Clinical Center if you had additional staffing. At what capacity is the Center operating? What percentage of available beds can be used given current staffing levels?

Dr. Wyngaarden. The Clinical Center is currently operating at approximately sixty-five percent occupancy. It should be noted that the primary mission of the Clinical Center is to support biomedical research as it evolves rather than to serve the health needs of all the patients who could be crowded into its rooms; our objective is to give the best possible care to the specific patients who have been recruited and have volunteered to take part in study protocols.

Mr. Early. Are there additional research projects or studies that could be expanded at the Center if you had more staff resources? What types of projects would these be and what additional resources would be necessary? Could you do more work on AIDS at the Clinical Center if additional staff were available?

Dr. Wyngaarden. The Clinical Center could effectivily use additional resources. Examples include specially isolated clinic rooms for studies of herpes zoster, nuclear medicine instruments for the study of the density of bones with osteoporosis, nurses to provide the intensive care needed by patients undergoing certain forms of cancer treatment, and personal computers integrated with the hospital Medical Information System to allow daily charting of AIDS patient findings.

ACQUIRED IMMUNE DEFICIENCY SYNDROME

Mr. Early. Funds for FY87 NIH AIDS activities are being requested in a newly proposed account for the Office of the Assistant Secretary of Health. Of the $203.482 million being requested, how much is for NIH activities?

Dr. Wyngaarden. The NIH currently anticipates reimbursements totalling $142,990,000 in FY 1987 from the proposed OASH appropriation.

Mr. Early. Of this amount how much is planned for extramural activities, and how much for intramural activities? How many FTE's are associated with the intramural portion?

Dr. Wyngaarden. Of the $142,990,000 in anticipated reimbursements, we estimate that 78 percent will be obligated in extramural areas, and 22 percent in the intramural research program. A total of 235 FTEs are anticipated to be involved in the NIH AIDS program in FY 1987: 148 in intramural research, 29 in research management and support, and 58 at the Clinical Center.

Mr. Early. What portion of this amount is for ongoing commitments? What portion is for new activities? Expansion of current activities?

Dr. Wyngaarden. Approximately $131.9 million will support ongoing commitments and expansion of current activities, and $11.1 million will fund new efforts.

Mr. Early. Doctor, what portion of the FY87 requested amount for AIDS reflects funds and FTE's that have been redirected or reprogrammed from other research areas and activities, including those that were not originally identified or designated as "pure AIDS" research per se? Provide for the record a table showing the amounts and number of FTE's that have been redirected to AIDS research from other areas for FY82 through FY86 inclusive. Also include any amounts that you plan to redirect in FY87. Also, please indicate from which research areas/programs these funds were/are redirected.

Dr. Wyngaarden. It is not possible to estimate the resources that have been redirected to the AIDS research program. Over the years, our programs have appropriately shifted to AIDS as we recognized its importance as a major infectious disease. At this stage, we cannot identify the specific impact on each activity that has been affected by this redirection.

Mr. Early. Please provide for the record a table (or tables) displaying by Institute and in the aggregate the following: The amount of NIH's share of the FY87 AIDS request for extramural programs and intramural programs (including associated FTE's); the amounts associated with ongoing commitments in each of the above categories; the amount of new money being requested in extramural and intramural; the amounts that represent previous or current redirection of reprogramming of funds and FTE's from other than AIDS activities for both extramural and intramural activities. Also, please provide a similar table (or tables) for FY86.

Dr. Wyngaarden. The tables on the following pages display the majority of the information you have requested; the remainder of the data cannot be reconstructed.

Mr. Early. Are funds for AIDS research activities at the Clinical Center included in the OASH request? If so, how much and how many FTE's.

Dr. Wyngaarden. Funding for AIDS research activities at the Clinical Center are contained within the Institute appropriations and are therefore included in the OASH request, albeit not as a line item. Approximately 58 FTEs will be involved in AIDS activities at the Clinical Center in FY 1987.

National Institutes of Health

1986 CURRENT ESTIMATE: AIDS FUNDING BY MECHANISM
(Dollars in Thousands)

	NCI		NHLBI		NIDR		NINCDS	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research Grants:								
Research Projects:								
Noncompeting	[illegible]	[illegible]	[illegible]	[illegible]				
Administrative Supplements								
Competing	[illegible]	[illegible]			1	$97	1	$173
Subtotal	[illegible]	[illegible]	[illegible]	[illegible]	1	97	1	173
Research Centers:								
Specialized		[illegible]		[illegible]				
Other								
Clinic								
Subtotal		[illegible]		[illegible]				
Other Research:								
Careers								
Cooperative Clinical	[illegible]	[illegible]						
MBRS								
Other			1	122				
Subtotal	[illegible]	[illegible]	1	523				
Total, Grants		4,037		1,760		97		173
Training:								
Individual								
Institutional								
Total								
Contracts	[illegible]	17,091	6	8,867				
Intramural		19,470				$1,415		1,262
RMS		70		91		200		
Total, 1986		40,668		10,718		1,712		1,435

National Institutes of Health

1986 CURRENT ESTIMATE: AIDS FUNDING BY MECHANISM - Continued
(Dollars in thousands)

	NIAID		NEI		DRR		TOTAL	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research grants:								
Research Proj.:								
Noncompeting	37	4,756					100	$12,532
Admin. suppl.								
Competing	19	3,397					28	4,024
Subtotal	56	8,153					128	16,556
Research Ctrs.:								
Spec/comp.		[illegible]						923
GCRCs						373		373
LASPR						1,089		1,089
Subtotal		[illegible]				1,462		2,385
Other Res:								
Careers	1	62					1	62
Coop.Cl.							3	1,500
BRS						195		195
Other	1	1,530					1	2,023
Subtotal	2	1,592				195	5	3,780
Total, RG		9,997				1,657		22,721
Training:								
Individual								
Institutional	1	123					1	123
Total	1	123					1	123
Contracts	96	38,170					99	64,128
Intramural		10,883		996				28,126
RMS		2,257						2,618
Total, IRD		61,430		996		1,657		117,716
				Office of the Director				3,041
				TOTAL, NIH				120,757

National Institutes of Health

1987 ESTIMATE: AIDS FUNDING BY MECHANISM
(Dollars in thousands)

	NCI		NHLBI		NIDR		NINCDS		NIAID	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research Grants:										
Research proj.:										
Noncompeting	[illegible]	[illegible]			[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	34,262
Administrative supplements										
Competing	[illegible]	[illegible]	8	[illegible]	1	[illegible]			15	6,768
Subtotal	[illegible]	[illegible]	8	[illegible]	1	[illegible]	1	[illegible]	[illegible]	[illegible]
Research ctrs.:										
Specialized		[illegible]								296
Clinical										
Comprehensive										
Subtotal		[illegible]		[illegible]						296
Other res.:										
Careers									2	63
Cooperative	[illegible]	[illegible]								
MBRS										
Other			1	[illegible]					2	[illegible]
Subtotal	[illegible]	[illegible]	1	[illegible]					5	1,628
Total, RGs		[illegible]		[illegible]		[illegible]		[illegible]		[illegible]
Training:										
Individual										
Institutional									1	108
Total									1	108
Contracts	42	[illegible]	8	[illegible]	1	[illegible]			57	41,674
Intramural		16,121				1,768		1,417		12,029
RMS				110		265				3,155
Total, [illegible]		47,151		[illegible]		[illegible]		1,575		97,520

National Institutes of Health

1987 ESTIMATE: AIDS FUNDING BY MECHANISM - Continued
(Dollars in thousands)

	NICHD		NEI		DRR		TOTAL	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research grants:								
Research Proj.:								
Noncompeting							76	$12,385
Admin. suppl.								
Competing							47	7,021
Subtotal							123	19,406
Research Ctrs:								
Spec/comp.								993
GCRCs						$399		399
LASPR						5,536		5,536
Subtotal						5,935		6,928
Other Res:								
Careers							1	65
Coop.Cl.							3	1,500
BRS						207		207
Other							3	2,097
Subtotal						207	7	3,869
Total, RG						6,142		30,203
Training:								
Individual								
Institutional							1	108
Total							1	108
Contracts	2	$674					108	77,690
Intramural				$104				31,459
RMS								3,530
Total, NIH		674		104		6,142		142,990

National Institutes of Health

AIDS — FTEs

FY 1986 ESTIMATE

	Intramural	Research Management and Support	Total
NCI	92	6	98
NHLBI	0	1	1
NIDR	4	0	4
NINCDS	16	0	16
NIAID	36	21	57
NEI	0	0	0
DRR	0	0	0
Subtotal	148	28	176
Clinical Center			58
TOTAL			234

National Institutes of Health

AIDS — FTEs

FY 1987 ESTIMATE

	Intramural	Research Management and Support	Total
NCI	92	6	98
NHLBI	0	2	2
NIDR	4	0	4
NINCDS	16	0	16
NIAID	36	21	57
NEI	0	0	0
DRR	0	0	0
Subtotal	148	29	177
Clinical Center			58
TOTAL			235

HEALTH AND BEHAVIOR

Mr. Hoyer. Mr. Nicholas, the Senate subcommittee included language in its report last year on health and behavior and the establishment of an inter-institute task force on this subject. The Senate requested a report of this subject. Has the report been completed? What are the major findings of the Report? Recommendations?

Mr. Nicholas. The report on the establishment of an inter-Institute task force on behavioral research, as requested by the Senate Appropriations Committee, was completed and forwarded to the Committee prior to the FY 1987 hearings.

In the report it is stated that "In 1981 an inter-Institute 'Working Group on Health and Behavior' was established by the Acting Director, NIH, to consider issues of health and behavior. These issues involve a broad range of behavioral and social science approaches, and include the potential for modifying lifestyle in ways that could help reduce morbidity and mortality.

The NIH Working Group on Health and Behavior undertakes to provide a forum for communication and for development of programs. In order to share the latest scientific information and to stimulate programmatic efforts, the Group has conducted well-attended NIH seminars on topics ranging from compliance in clinical trials and the physician as a behavioral change agent; to behavioral factors in hypertension, cancer, and AIDS; to an entire series on health promotion through interventions in smoking behavior in schools, the workplace, the female population, and the population of heavy smokers. The Group has held discussions on Requests for Application and Program Announcements in advance of their issuance, (as on Behavioral Pediatrics, NICHD, and Behavioral Geriatrics, NIA)..." and is actively encouraging research proposals related to health and behavior. "It has reported to the Director, NIH, on such issues as the recommendations from the Institute of Medicine Study and the plans for the PHS initiative on health and behavior. Among its current activities are plans for integrating information and findings from the diverse NIH studies in this area, and for communicating these developments to other scientists and to the larger community."

RESCISSION

Mr. Hoyer. Mr. Nicholas, your office has a rescission request pending for $9,140,000. What activities or efforts will be eliminated based on this request?

Mr. Nicholas. The pending rescission of $9,140,000 will be applied to the programs that support biomedical research in small and minority schools and universities. These are the Academic Research Enhancement Awards (AREA) Program and Research Centers in Minority Institutions (RCMI) Program. The level available for these programs after the rescission will be $5 million each, a continuation of the 1985 levels.

STAFF MORALE

Mr. Hoyer. Generally, Mr. Nicholas, do you believe that there is a problem with staff morale at the NIH? H-19

Mr. Nicholas. No, I do not believe there is a staff morale problem at this time.

REORGANIZATION OF THE OFFICE OF RESEARCH SERVICES

Mr. Hoyer. I believe there were three (3) divisions in the Office of Research Services prior to the reorganization, the Division of Safety, the Division of Engineering Services and the Division of Administrative Services. Under the new structure, you have split the Division of Administrative Services into three divisions and created a fourth division from an office that was originally a branch of the Division of Administrative Services. Tell me Doctor, if this reorganization was done to achieve efficiency, to eliminate duplication, decrease operating expense, and cut overhead cost, how has the creation of four new divisions done so. I would think that this would increase rather than decrease the overall operating expense of your office. How has it increased efficiency? H-20

Dr. Becker. Under the old Division of Administrative Services there were 20 individuals involved in management of the Division and its ten branches (Division Director, Management Assistant to the Director, 2 Assistant Directors, 2 Deputy Assistant Directors, 10 Branch Chiefs and 4 Assistant Branch Chiefs). With the new organization there are 12 individuals (11 currently on board) responsible for such management (3 Division Directors, 1 Assistant Director, 7 Branch Chiefs and no Assistant Branch Chiefs; plus the Chief, Security Branch, which was transferred to the Division of Safety). This reduction of 40 per cent in the number of upper and mid-level managers provides direct cost savings in salaries and benefits for these positions (estimated at $400,000).

Mr. Hoyer. Since the reorganization was done to achieve efficiency and effect cost savings, what are the cost comparisons before and after the reorganization in such areas as supply management, property management, procurement, security, printing, transportation, and communications? H-21

Dr. Becker. The reorganization of the Division of Administrative Services was effective March 16, 1986. The cost savings that are known to date are those associated with the administrative layers that no longer exist under the new organization. These are detailed above. If further savings occur in the specific activities, such as supply, property, procurement, printing, etc., it will be impossible to identify those accruing from the reorganization vs. those from FTE reductions, implementation of new techniques, or improved management. Many of these activities are operated on a fee-for-service basis and the NIH "marketplace" figures prominently in establishing the level of their costs. This is a dynamic process involving the demand for services, the cost of services, and the rate of user charge. With the current budgetary constraints on spending, demand for service may drop and activity managers will have to reduce costs in the long run, none of which has much to do with the divisional hierarchy.

The reorganization eliminated unnecessary administrative layering and established a leaner management structure even though more divisions now exist. The cost savings are those outlined; others expected cannot be identified at this time or linked specifically to the reorganization. That action created the managerial environment in which future savings might occur through other factors at work.

Mr. Hoyer. Are these services now more economical to the institutes than they were before?

Dr. Becker. I believe that ORS services overall are more economical than they were two years ago, but it is difficult to document the savings in detail. Often the greatest savings to NIH as a whole result from an improvement in the quality or responsiveness of the service, which permits more efficient conduct of research, yet is not immediately apparent as a measurable saving.

Direct cost savings, such as those resulting from elimination of managerial echelons, are easy to measure. However, the bulk of the expenses depend heavily on demand by the Institutes for services and on factors outside our control. For example, we have increased security coverage in the Clinical Center, which resulted in an increase in costs; our telecommunications costs have risen because of increased usage, particularly in data transfer, and rate increases and new user charges imposed by the telephone systems; and we must now pay more for disposal of radioactive and other hazardous wastes. Nevertheless, in certain areas where the costs of providing goods or services is recovered from direct user fees we have seen significant decreases. For example, the cost of providing supplies from our central and self-service stores decreased from 20 per cent of the cost of the supplies to 10 per cent, while the speed of delivery from the warehouse to the scientists needing supplies was improved from typical 2-3 week delays to 48 hour service. Our printing services are in transition from the use of outdated technology and large staffs to modern high-speed automated equipment. Projections indicate that we will achieve substantially lower costs, with better quality control and shorter turn-around times. The ORS report in December, 1985 on our improvements in productivity listed many examples of such economies that have been achieved.

Mr. Hoyer. Would you give me the budget for the Office of Research Services for each year since 1983? Has it increased or decreased? # 22

Dr. Becker. The following table provides the actual obligations of the Office of Research Services for the years 1983-1985 and estimates for 1986 and 1987. Figures are not comparable because of changes in accounting for the costs of central services between 1986 and 1987.

OFFICE OF RESEARCH SERVICES
Actual Obligations, 1983-1987
(Dollars in Millions)

1983	1984	1985	1986 Estimate	1987 Estimate
125.4	128.5	137.8	164.9	173.0

MINORITY EMPLOYMENT UNDER REORGANIZATION

Mr. Hoyer. Compare the cost of this reorganization in human factors, for example how many black Directors, Deputy Directors, Branch Chiefs, Section Chiefs, Administrative and Budget Officers did you have in 1983 and how many do you have now? # 30

Dr. Becker. At the end of 1983 the Division of Administrative Services had 19 blacks in the positions listed; (1 Division Director, 2 Assistant Directors, 2 Branch Chiefs, 11 Section Chiefs, 2 Administrative Officers, and 1 Budget Officer); at present in the components that have evolved from DAS there are 18 blacks in comparable positions (0 Division Directors, 1 Assistant Director, 3 Branch Chiefs, 12 Section Chiefs, 2 Administrative Officers, and 0 Budget Officers). Since the number of such positions has decreased from 50 to 41, the percentage of blacks is slightly higher than in 1983.

REORGANIZATION OF THE OFFICE OF RESEARCH SERVICES

Mr. Hoyer. Describe your involvement with the Division of Administrative Services Equal Opportunity Office and Affirmative Action Program before and after the reorganization. Do you have an affirmative action plan?

Dr. Becker. Prior to the reorganization of the Division of Administrative Services (DAS), I was the Acting Division Director. As such, I met on a recurring basis with the DAS Affirmative Action Committee and with the DAS Equal Employment Officer. The EEO Officer and the Committee chairperson were free to discuss any matters of importance to the EEO program with me, and did so frequently. During this period, DAS revised its Affirmative Action Plan (AAP) for the Division. This plan was developed with my input and concurrence. The reorganization of DAS occurred at a time when the implementation of the AAP was just beginning.

Realizing that the newly established divisions within the Office of Research Services (ORS) had no established EEO committees or AAPs, I have taken two remedial actions. First, I have established, in conjunction with the Office of the Director, NIH (OD), a consolidated EEO office, staffed with employees formerly assigned to the ORS divisions. This office will provide leadership to all of OD and ORS in the establishment and maintenance of an EEO program. This office provides the EEO program a level of management support and visibility it had not had previously. In addition, for the first time, OD will receive the benefit of an office devoted to the oversight of the EEO program. Second, I have established an ORS EEO Advisory Committee. The purpose of the committee is to deal with ORS-wide EEO activities and employee concerns. This committee will interface with division-level committees, which will provide the local representation necessary for the success of the EEO program. This network of committees will assist the new EEO Office in the development of an OD/ORS AAP. The former DAS AAP, as well as those of the Division of Safety and the Division of Engineering Services, will serve as a guide for the development of the ORS plan, and many of the action items from the DAS plan will be retained.

CONTRACTING OUT

Mr. Hoyer. I believe you stated last year that several functions under your office were being scheduled for contracting out or were already contracted out to cut cost and improve efficiency. Would you compare the cost of all of the functions that have been contracted out, specifically housekeeping services, guard services and supply and delivery, with the cost of these functions when they were performed in-house by federal employees. 426

Dr. Becker. The Office of Research Services has not contracted completely the performance of the services listed, in fact, some of those have not been contracted at all. Because of the FTE constraints in effect at the NIH, we have viewed the contract mechanism as a valuable option in augmenting services performed by employees. Such is the case with guard services. Early in FY 1985, it became apparent that the NIH needed to increase security within the Clinical Center. This could only be accomplished by enlarging police/security resources. Internal hiring restrictions precluded the expansion of FTEs. After a thorough review of all NIH facilities, the NLM complex was selected as best suited for the use of contract guard services. A decision was made to reassign the existing staff at the National Library of Medicine to the Clinical Center and to contract for guard services to maintain security at the NLM. An excellent minority contractor, who was already providing guard services at two off-campus sites, was selected to provide this service. The contract cost of this in FY 1985 (1/85-9/85) was $354,000. This compares with the estimated government cost, in salaries only, of $184,166. Even with an estimate for overhead added to the government cost, the contract cost may still be higher or comparable, but an additional 15-16 FTEs would have been required.

Similarly, in the case of housekeeping services, constraints on hiring and demands for improved services from the NIH community combined to make contracting a viable tool. Up until 1985, the use of overtime was relied on to accomplish the housekeeping function and, even then, many complaints were received about the quality of service. A minority contractor was employed to service Buildings 1 and 31, the campus' two main administrative buildings; the contract cost was approximately $500,000 on an annual basis, only slightly higher than the government's cost. The occupants of these buildings have overwhelmingly approved the contractor's service. The use of contracts was extended recently to Buildings 38 and 38A, administrative buildings at the National Library of Medicine. The federal employees in housekeeping services have been redirected to the service of the campus' laboratory buildings, where specialized care is needed.

Regarding the supply function, no contracts have been established in lieu of federal employment and, in the delivery function, no new aspects have been contracted besides those that have been in existence for years.

Mr. Hoyer. What impact has contracting out had on entry-level jobs previously held by minorities. Specifically housekeeping, mail and messenger services, truck drivers, warehousemen, etc. How many of these jobs did you have before and how many do you have now?

Dr. Becker. Although reviews are being conducted under OMB Circular A-76, we have not contracted out for mail and messenger services, truck drivers or warehouse workers. Therefore, there has been no effect on the number of positions in these occupations. Housekeeping services for off-campus rental buildings have always been done by contract. In addition, housekeeping in several administrative buildings at NIH has been contracted out, as the housekeeping staff declined through attrition. Thus, it has been unnecessary to take any involuntary actions to reduce the staff.

Clearly, as we have moved more of our housecleaning under contract, the number of future Government entry-level jobs in this area has decreased. Our total housekeeping staff has declined from 138 in 1983 to 118 at present.

Mr. Hoyer. Would you provide for the record, the disposition of all ORS functions that were originally on the NIH A-76 inventory. # 27

Dr. Becker. The disposition of ORS functions that were on the A-76 inventory at the time ORS was formed (1980) is as follows:

Housekeeping - Removed from the A-76 Inventory since it is not one of the 14 categories identified by OMB for review.

Fire Prevention - An RFP was issued in 1983, but no bids were received. The function was removed from the A-76 Inventory since it is not one of the 14 categories identified by OMB for review.

Audio-Visual - An RFP has been issued. However, as a result in the declining use of audio-visual services, the statement of work is no longer accurate. The RFP will be cancelled, and the future of audio-visual services reconsidered.

Groundskeeping - A Sources Sought Synopsis was issued in 1982; however, no satisfactory sources were available. The function remains on the A-76 Inventory and will be reviewed again in 1987.

Elevator Maintenance - The solicitation for an RFP was closed in February, 1986. No bids were received.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

Office of the Director

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OFFSET
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NATIONAL INSTITUTES OF HEALTH

Office of the Director

For carrying out the responsibilities of the Office of the Director, National Institutes of Health, [$117,085,000] *$36,707,000*, including purchase of not to exceed [ten] *six* passenger motor vehicles for replacement only. (*Department of Health and Human Services Appropriation Act, 1986.*)

NATIONAL INSTITUTES OF HEALTH

Office of the Director

Amounts Available for Obligation 1/

	1985	1986	1987
Appropriation	$38,304,000	$117,085,000	$ 36,701,000
Enacted administrative reduction	---	-93,000	---
Sequester order	---	-5,031,000	---
Proposed rescission	---	-23,055,000	---
Subtotal, adjusted appropriation	38,304,000	88,906,000	36,701,000
Comparative transfer to:			
Office of the Assistant Secretary for Health, for AIDS Project		-53,075,000 2/	
National Heart, Lung, and Blood Institute (for changes in the Central Services financing mechanism and formulas)	-540,000	---	---
National Institute of Dental Research (for changes in the Central Services financing mechanism and formulas)	-353,000	---	---
National Institute of General Medical Sciences (for changes in the Central Services financing mechanism and formulas)	-324,000	---	---
Subtotal, adjusted budget authority	37,087,000	35,831,000	36,701,000
Unobligated balance, start of year	---	2,779,000	---
Unobligated balance, end of year	-2,779,000	---	---
Unobligated balance, lapsing	-129,000	-2,000	---
Total obligations	34,179,000	38,608,000	36,701,000

1/ Excludes the following amounts for reimbursable activities carried out by this account: 1985 -- $10,025,000; 1986 -- $14,457,000; 1987 -- $15,407,000.

2/ The comparative amount for the appropriation is $70,000,000 and $66,990,000 for the sequestration.

Office of the Director

Budget Mechanism

(Dollars in thousands)

	1986 1/2/ Appropriation	1986 1/3/4/ Available after sequestering	1986 1/3/5/ Revised		1987	
	Amount	Amount	FTEs	Amount	FTEs	Amount
Research Management and Support............	$ 49,771	$ 44,748	519	$38,608	519	$36,701

1/ Reflects an enacted administrative reduction of $93,000, and a carryover in unobligated funds of $2,779,000.

2/ Reflects a comparative transfer of $70,000,000 to the office of the assistant Secretary of Health for AIDS project

3/ Reflects a consultant services (Section 515 of the Treasury-Postal Services Appropriation Act, 1985) withholding of $2,000.

4/ Reflects a comparative transfer of $66,990,000 to the Office of the Assistant Secretary of Health for AIDS project.

5/ Reflects a comparative transfer of $53,075,000 to the Office of the Assistant Secretary of Health for AIDS project.

NATIONAL INSTITUTES OF HEALTH

Office of the Director

CROSSWALK - 1986 Appropriation

(Dollars in thousands)

PROGRAM ACTIVITY	MECHANISM Research Management and Support	Total
Research Management and Support	$ 49,771	$ 49,771
Total	49,771	49,771

NATIONAL INSTITUTES OF HEALTH

Office of the Director

CROSSWALK - 1986 Available After Sequestering

(Dollars in thousands)

PROGRAM ACTIVITY	MECHANISM Research Management and Support	Total
Research Management and Support	$ 44,748	$ 44,748
Total	44,748	44,748

NATIONAL INSTITUTES OF HEALTH

Office of the Director

CROSSWALK - 1986 Revised Estimate

(Dollars in thousands)

	MECHANISM	
PROGRAM ACTIVITY	Research Management and Support	Total
Research Management and Support	$38,608	$38,608
Total	38,608	38,608

NATIONAL INSTITUTES OF HEALTH

Office of the Director

CROSSWALK - 1987 Congressional Justification

(Dollars in thousands)

PROGRAM ACTIVITY	MECHANISM	
	Research Management and Support	Total
Research Management and Support	$36,701	$36,701
Total	36,701	36,701

Office of the Director

Summary of Changes

1986 Current estimated obligations..............................	$ 38,608,000
1987 Estimated obligations..	36,701,000
Net change..	-1,907,000

	1986 Base	Change from Base
Increases:		
A. Built-in:		
1. Within grade increase.......	$20,117,000	+304,000
2. Federal Employees Compensation Fund increase	86,000	+25,000
3. FTS rate increase...........	219,000	+9,000
4. Payment for centrally furnished services........	3,144,000	+141,000
5. Increased cost of laboratory supplies, materials and other expenses............	2,457,000	+391,000
Subtotal............	---	+870,000
Decreases:		
A. Program:		
1. Research management and support: Program decrease in lower priority areas.....	18,491,000	-2,777,000
Subtotal............		-2,777,000
Total, net change...............		-1,907,000

Office of the Director

Budget Authority by Activity
(Dollars in thousands)

	1986 1/2/ Appropriation	1986 1/3/4/ Available after sequestering	1986 1/3/5/ Revised		1987	
	Amount	Amount	FTEs	Amount	FTEs	Amount
Research management and support.......	$ 49,769	$ 44,748	519	$38,608	519	$36,701
Total obligations...	49,769	44,748	519	38,608	519	36,701
Unobligated balance, lapsing...........	---	---	--	---	--	---
Total budget authority.........	49,769	44,748	519	38,608	519	36,701

1/ Reflects an enacted administrative reduction of $93,000, and a carryover in unobligated funds of $2,779,000.

2/ Reflects a comparative transfer of $70,000,000 to the Office of the Assistant Secretary of Health for AIDS project.

3/ Reflects a consultant services (Section 515 of the Treasury-Postal Services Appropriation Act, 1985) withholding of $2,000.

4/ Reflects a comparative transfer of $66,990,000 to the Office of the Assistant Secretary of Health for AIDS project.

5/ Reflects a comparative transfer of $53,075,000 to the Office of the Assistant Secretary of Health for AIDS project.

Office of the Director

Obligations by Object

	1985 Actual	1986 Estimate	1987 Estimate
Total Number of Full-Time permanent positions.................	529	501	501
Total compensable workyears: Full-time equivalent employment.......	583	536	536
Full-Time equivalent of overtime and holiday hours..................	3	3	3
Average ES salary.....................	$66,232	$62,920	$62,920
Average GS grade......................	9.14	9.14	9.14
Average GS salary.....................	$28,224	$26,813	$26,813
Average salary, grades established by act of July 1, 1944 (42 USC 207).	$35,361	$33,593	$33,593
Average salary of ungraded positions..	---	---	---
Personnel compensation:			
Permanent positions..................	16,320,000	16,245,000	16,475,000
Positions other than permanent......	1,335,000	1,335,000	1,409,000
Other personnel compensation........	229,000	178,000	178,000
Special personnel compensation......	83,000	18,000	18,000
Subtotal, personnel compensation..	17,967,000	17,776,000	18,080,000
Personnel benefits....................	2,095,000	2,341,000	2,366,000
Travel and transportation of persons..	223,000	167,000	173,000
Transportation of things..............	3,000	5,000	5,000
Rent, communications and utilities....	687,000	647,000	683,000

Printing and reproduction.............	289,000	209,000	218,000
Other services:			
Centrally furnished services........	5,141,000	3,144,000	3,285,000
Standard level user charge..........	---	---	---
Other................................	8,099,000	13,977,000	11,535,000
Supplies and materials................	283,000	176,000	183,000
Equipment.............................	609,000	166,000	173,000
Total........................	35,396,000	38,608,000	36,701,000

Office of the Director

Significant Items in House Appropriations Committee Report

Items	Action Taken or to be Taken
Acquired Immune Deficiency Syndrome	
1. "The Committee is providing an additional $70 million within the appropriation of the Office of the Director for the Director, NIH, to disburse among the Institutes for new AIDS initiatives and expanded programs. The Committee intends that whatever additional staffing is required for the AIDS research effort and its intensified management should be provided." (p. 35)	1. A report on the distribution of the $70,000,000 for AIDS research will be submitted to the House. In applying the 1986 FTE ceiling among the institutes, AIDS positions were protected.
Clinical Center Staffing	
2. "The Committee has been informed that the patient care activities at the Warren Magnuson Clinical Center are seriously understaffed. The Committee requests that the Secretary of Health and Human Services and the Director, NIH, take immediate steps to correct this situation." (p. 36)	2. Dr. Wyngaarden acknowledged in his memorandum of November 12, 1985, to the Honorable William H. Natcher that the staff of the Clinical Center is adequate to ensure quality care.

Office of the Director

Significant Items in Senate Appropriations Committee Report

Items	Action Taken or to be Taken
Office of Management and Budget	
1. "NIH is directed to disregard OMB substantive directions on the use of apportioned funds. Also, the Committee reminds the Director of NIH and the Directors of the various Institutes that they retain the responsibility to authorize minor shifts in subaccount budget authority to take advantage of unanticipated research opportunities. The Committee expects this authority to be used, as appropriate." (p. 57)	1. NIH is cognizant of the authority to make funding shifts between activities and has used this authority in the past when appropriate.
Small Business Innovation Research	
2. "The Committee expects the Director will provide strong central management and representation for the SBIR Program and the Director will be responsible for ensuring that special emphasis be given to the following objectives: (1)... (2)... (3)... The Committee directs that these objectives be realized during the 1986 fiscal year." (p. 57)	2. The Office of the Director oversees the solicitation for SBIR applications, allocates the SIBR assessement to BIDs, monitors actual obligations and prepares all SBIR financial reports. The Director is committed to the objectives of the SBIR program as outlined by the Committte and ensures that these objectives will be met in FY 1986.

Behavioral Research

3. "The Committee requests the Director of the NIH to establish a special inter-Institute task force on behavioral research, in order to ensure that an appropriate priority is given to this evolving area by each of the Institutes and to provide the Director and the Committee with guidance in this area for next year's bill." (p. 112-113)	3. An inter-Institute task-force on behavioral research has been established and in operation since December, 1981. This working group, the "NIH Working Group on Health and Behavior," has representatives from all Institutes; holds monthly meetings; stimulates the development of programmatic and scientific information; and makes recommendations to the Director, NIH, as appropriate. A report on this topic will be submitted to the Committee as requested.

Office of the Director

Appropriations History

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation [1]
1978	18,923,000	18,900,000	18,900,000	18,900,000
1979	20,157,000	20,457,000	20,457,000	20,457,000
1980	21,969,000	21,062,000	21,062,000	21,036,000
1981	23,236,000	22,549,000	22,634,000	22,531,000
1982	20,682,000	36,502,000	23,502,000	23,618,000
1983	24,283,000	24,683,000	24,683,000	24,683,000
1984	26,720,000	26,779,000	26,720,000	26,720,000
1985	27,509,000	47,509,000	38,304,000	37,087,000[2]
1985 Proposed Recission	-182,000			
1986	37,085,000	117,085,000	37,574,000	116,992,000[3]
1986 Sequester	-5,031,000			
1986 Proposed Rescission	-23,055,000			
1987	36,701,000			

[1] Reflects enacted supplementals, rescissions, and reappropriations.

[2] Includes $10,000,000 for the initiation of a program that supports biomedical research in small and minority schools and universities.

[3] Includes $20,000,000 for the continuation of a program that supports biomedical research in small and minority schools and universities, and $70,000,000 for research on acquired immune deficiency syndrome (AIDS).

Office of the Director

Justification

	1986 Appropriation Amount	1986 Available After Sequestering Amount	1986 Revised FTEs	1986 Revised Amount	1987 FTEs	1987 Amount
Research Management and Support........	$49,771,000	$44,748,000	519	$38,608,000	519	$36,701,000
Total...........	49,771,000	44,748,000	519	38,606,000	519	36,701,000

General Statement

The appropriation for the Office of the Director of the National Institutes of Health (NIH) funds those components of the NIH that provide central administration and services to NIH Bureaus, Institutes, and Divisions. Chief among these components is the immediate Office of the Director, NIH, which is primarily responsible for the development and management of intramural and extramural research policy and the coordination of NIH scientific inquiry. A number of other offices are responsible for the provision of NIH-wide direction and centralized services in such areas as, communications, program planning and evaluation, equal opportunity, contract and grant administration, investigation and review, protection from research risks, and financial and personnel operations.

Overall Budget Policy

The 1987 budget request is $36,701,000, a decrease of $1,907,000 from the 1986 revised appropriation. This request includes funds for the continuation of the program initiated in 1985 that supports biomedical research in small and minority schools and universities. The program is designed to raise the proportionate share of the targeted institutions in the growth of the NIH extramural programs relative to the larger, more prominent universities. In FY 1987 all funding for AIDS research will be requested by the Office of the Assistant Secretary for Health. Therefore, the OD request for FY 1987 includes no funds for AIDS research. AIDS funding in the OD will be supported through a reimbursable agreement with OASH.

Program Accomplishments

During FY 1985, special emphasis was placed on several priorities in extramural research pertaining to the welfare of human subjects and animals in research, AIDS research, and the continuation and implementation of several Congressional directives. There has been continued development of policies and regulations for the protection of human subjects from research risks and the care and use of laboratory animals. In FY 1985, 290 Single Project Assurances were negotiated with research institutions throughout the nation and abroad to bring them into full compliance with the Department's regulations on human research subjects.

In collaboration with the Food and Drug Administration, the NIH has produced educational programs and has begun an audiovisual initiative for national use in educating institutional officials, researchers and institutional review board members in their responsibilities for protecting human subjects.

Improvement of procedures for ensuring the welfare of laboratory animals continues to be a major focus of the Office of the Director. In 1985 the OD published revised guidelines for the care and use of research animals, to take effect January 1, 1986. A program of announced and unannounced site visits to assess institutional compliance with animal welfare requirements will continue for the next three years, and a program of animal welfare education workshops, which was begun in 1985, will continue in 1986 with nine additional workshops.

In 1985, the OD continued its role in coordinating extramurally funded research on Acquired Immune Deficiency Syndrome (AIDS) and ensured that appropriate solicitations for research related to AIDS were processed expeditiously. New Congressional directives for Academic Research Enhancement Awards and Research Centers in Minority Institutions were launched. These and other established efforts, such as the Extramural Associates Program, are aimed at encouraging increased participation of minority and other under-represented groups of scientists and institutions in NIH research programs.

The Academic Research Enhancement Award Program (AREA) is intended to strengthen the research milieu of non-research-intensive, four-year colleges and universities that provide undergraduate training for a significant number of our nation's research scientists. Following scientific merit review and selection of projects for funding, AREA funds, which are part of the OD appropriation, are transferred to the individual BIDs for award and administration. AREA grants, which are non-renewable, provide up to $50,000 for direct costs (plus applicable indirect costs) for a period not to exceed 24 months. They enable qualified individual scientists within eligible institutions to carry out health-related feasibility studies, pilot studies and other small-scale research projects. In FY 1985, 75 AREA grants, totalling approximately $5 million, were awarded for research projects in educational institutions that have not been traditional recipients of NIH research funds.

The Research Centers in Minority Institutions Program (RCMI) was developed in 1985 to establish research centers in those predominantly minority institutions which offer doctoral degrees in the health professions or the sciences related to health. The Program acknowledges the historical role which minority educational institutions have traditionally played in training a large proportion of professionals who provide health care to the minority community. The RCMI grants are intended to enhance significantly the capacity of such institutions for the conduct of biomedical and/or behavioral research by strengthening and augmenting both their human and physical resources. The program began in FY 1985 and is administered by the Division of Research Resources on behalf of the Office of the Director, NIH.

Seven RCMI grants were awarded in FY 1985. The recipient institutions (a college of pharmacy, three medical schools, and three graduate schools) are located in the states of Tennessee, Georgia, Florida, and New York, as well as in Washington, D.C., and Puerto Rico. These awards will enable faculty expansion and enrichment, physical facility improvement, and other research-related activites including laboratory renovation and equipment that will help institutions develop state-of-the-art research capability in areas such as neurosciences, immunogenetics, and molecular genetics.

FY 1985 was a very successful year for another Congressionally directed program, the Small Business Innovation Research (SBIR) Program. With the introduction of contracts as an additional funding instrument, the Program expanded both in scope and purpose. The NIH awarded 249 Phase I and 54 Phase II grants as well as 150 Phase I contracts, totalling approximately $40 million.

In the area of technology assessment and transfer, seven Consensus Development Conferences were held in the past year involving limb-sparing treatment of certain sarcomas, the lowering of blood cholesteral, traveler's diarrhea, health implications of obesity, anesthesia and sedation in the dental office, electroconvulsive therapy in psychiatry, and adjuvant chemotherapy for breast cancer. Through such conferences, the safety and effectiveness of emerging or established technologies are assessed and communicated to clinicians and the interested public. In addition to these conferences, a statutorily required technology assessment meeting was conducted on the feasibility of establishing a national registry of volunteer bone marrow donors and collaboration with European countries conducting consensus development programs was continued.

Communication of biomedical knowledge advanced in 1985 through the development of a new format for the column "From the NIH" published in the Journal of the American Medical Association. The column now includes six to eight short items on NIH research findings and other topics of interest to physicians in clinical practice. The column is in its ninth year and reaches 351,000 readers in the U.S. plus an equal number through JAMA's foreign editions. Communicating science news to the general public continued through efforts such as Healthline, a service providing information on recent research advances to newspaper and magazine health columnists. Two issues were produced on health topics of interest to women which expanded the Healthline audience to the women's health network. A weekly 15-minute radio interview with NIH researchers was developed and is distributed periodically on tape cassettes to 400 stations and via satellite to 200 National Public Radio stations. Productions on areas of special health interest are provided the public such as the motion picture on rabies developed by NIAID and the Department of Public Health. This film, to be distributed during FY 1986, is particularly needed because of the increase in rabies during the past few years in the mid-Atlantic states.

Office of the Director

Research Management and Support

1987 Authorization: Indefinite.

Budget Authority:

1986 Appropriation	1986 Available after sequestering	1986 Revised Estimate	1987	Increase or decrease
$49,771,000	$44,748,000	$38,608,000 (FTEs: 519)	$36,701,000 (519)	-52,205,000 (--)

Purpose and Method of Operation

Coordination and direction of research are the primary responsibilities of the Office of the Director. The Office of Intramural Affairs provides leadership and overall administration of the intramural program of the NIH and the determination of the role of the intramural program as it relates to the NIH as a whole. The Office of Extramural Research and Training provides guidance to the bureaus, institutes and divisions on the development and management of extramural research and training programs. The office is responsible for establishing NIH extramural research and training program policy and procedures, reviewing program quality and effectiveness, and coordinating selected NIH-wide program activities. Ongoing activities include: formulating budget strategies and resource allocation activities affecting the extramural programs; advising on selection of funding instruments; providing guidance on grants administration policy and procedures; and overseeing the development, implementation, and evaluation of a comprehensive research manpower training and development program for NIH.

Closely associated with the efforts of these two offices are those of the Office of Medical Applications of Research and of the Office for Protection from Research Risks. The former serves as the coordinator of, and stimulus for NIH technology assessment and transfer activities. Toward this end, the office works closely with the bureaus, institutes and divisions of the NIH in the assessment of drugs, devices, and medical procedures with the ultimate goal of translating the results of biomedical research into knowledge that can be used effectively and in a timely fashion in the delivery of health services.

The Office for Protection from Research Risks administers various regulations pertaining to the protection of human subjects in research, approves and gives guidance to Institutional Review Boards established for the protection of human subjects, and administers the Department's Animal Welfare Policy. In addition to this office's routine review of assurance statements and compliance checks, and work on related regulations and guidelines, this office has initiated an educational program, in concert with the Food and Drug Administration, to improve the awareness of relevant groups as to their responsibilities under various protection oriented regulations.

There are several offices and divisions within the Office of the Director whose roles are more closely aligned with the administrative support of research and the research environment. Included are the Office of Research Services, that administers the engineering, safety, space, and general housekeeping functions of the intramural program. The Office of Communications coordinates the public affairs and other communications activities of the 16 Bureau, Institute and Division Offices concerned with communication, public affairs and scientific reports. In carrying out its coordination responsibilities, the office reviews and approves plans for all NIH publications, manuscripts, audiovisual materials and exhibits, as well as proposed articles and statements on policy and program matters by NIH officials.

The Office of Program Planning and Evaluation provides leadership for the program planning, evaluation, and legislative activities at NIH and provides staff support to the Director's Advisory Committee, a public group advising on broad matters of health science policy.

Of significant support to the extramural program of the NIH, is the Division of Contracts and Grants that recommends NIH-wide contracting policies, reviews the contracting operations of the various NIH components to ensure compliance to policies, and conducts and monitors programs in contract and grant compliance to Small Business and Civil Rights legislation.

The remaining Divisions provide administrative services to NIH operating components in the areas of budget formulation and personnel management, equal opportunity compliance, review and analysis of NIH management policies, and survey and review of NIH awardees. The accounting functions provided include financial analysis and reporting; accounting, auditing, and processing of vouchers for more than a thousand cost centers; payment of 350-410,000 invoices per year; settlement of all types of claims; and development of more effective accounting and financial management systems. The personnel functions provided include development of personnel policy, planning, and implementation of personnel management evaluation programs, establishment of goals in the classification and compensation, staffing, and labor and employee relations programs, and administration of a personnel management information and publication system. Also provided are the overall direction and coordination of operational functions, central to which are the processing of over 20,000 requests for personnel actions during the year. Finally, training assistance, career development, and guidance and counselling are provided.

The Office of the Director's share of payments for centrally furnished services includes funds for such activities as maintenance of buildings and grounds, custodial services, communications, and transportation. Also included in this activity is the Office of the Director's share of payments to the General Services Administration for Standard Level User Charges.

Rationale for the Budget Request

The 1987 budget request of $36,701,000 for research and management support reflects $10 million for the continuation of the program initiated in 1985 that supports biomedical research in small and minority schools and universities. The 1987 budget request will permit the Office of the Director to continue to serve as an instrument for furthering and administering intramural and extramural biomedical research programs.

Extramural program management efforts will continue to focus on issues related to laboratory animal welfare and misconduct in science; further refinement of the peer review appeals process; and application of the Competition in Contracting Act (CICA) to R&D contracting procedures. The OD will explore ways of addressing the needs of new, established, and mid-career investigators as well as coordination of high-priority initiatives directed at identified health problems such as AIDS. Staff will also devote considerable efforts to implementation of the Health Research Act of 1985, particularly those provisions affecting peer review, scientific fraud, and use of animals in research.

Efforts will continue to disseminate educational materials, conduct workshops and participate in various kinds of public fora to sensitize the research community and the general public as to the requirements of regulations and PHS policies regarding human and animal subjects. Staff responsible for monitoring compliance to animal protection regulations will carry out site visits to awardee institutions conducting research involving animals. Depending on the circumstances, site visits may be announced or unannounced.

The consensus development initiative will continue at a level of six to eight conferences per year and focus on such topics as health implications of smokeless tobacco use, prevention of venous thrombosis and pulmonary embolism, the management of pain, and infantile apnea and home monitoring. These conferences will aid in furthering the knowledge and practice of medical practitioners and insure public awareness of such subjects. During 1987 the OD hopes to introduce the use of electronic media for the transfer of technology assessment and explore the possibility of introducing teleconferencing of concensus conferences.

The Office of Communication will continue to coordinate with 16 Bureau, Institute, and Division offices the activities concerned with communications, public affairs, and scientific reports. The office will continue to emphasize information activities in support of disease prevention research. Several crosscutting issues for emphasis in the coming year are the use of animals in research, AIDS research, and NIH's role in the "biotechnology era." Writer's seminars will be conducted on such topics as human gene therapy and greater attention will be placed on developing on-line information services and telephone message services.

Other central NIH offices will continue to emphasize improvements in the effectiveness and economy of operations. A comprehensive training program will be implemented to assure effective implementation of the Affirmative Action Program and the Federal Equal Opportunity Recruitment Program for minorities, women, handicapped individuals and disabled veterans. Monitoring of the efforts to implement the OMB Circular A-76 will continue as well as identifying, reviewing and ensuring responsiveness to the President's Reform 88 initiatives and to Departmental initiatives on productivity.

With the passage of the Competition in Contracting Act, the contracts and grants office will continue to coordinate the NIH implementation of significant changes to the Federal Acquisition Regulation, HHS Acquisition Regulations, and the PHS Acquisition Regulations. The Division of Financial Management will continue its improvements in both automated budget estimating techniques and financial systems design. In the area of personnel operations, the Division of Personnel Management expects to begin installation of a modernized DHHS personnel/payroll system and develop a comprehensive staffing and classification assessment methodology utilizing an extensive array of computer-generated data.

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Office of the Director

Detail of Permanent Positions

	1985 Actual	1986 Estimate	1987 Estimate
ES-5	3	3	3
ES-4	9	9	9
ES-3	0	2	2
ES-2	1	1	1
Subtotal	13	15	15
GS/GM-15	30	27	27
GS/GM-14	52	48	48
GS/GM-13	96	92	92
GS-12	47	45	45
GS-11	33	30	30
GS-10	6	6	6
GS-9	39	36	36
GS-8	21	17	17
GS-7	62	58	58
GS-6	58	57	57
GS-5	33	34	34
GS-4	18	15	15
GS-3	9	9	9
GS-2	5	5	5
Subtotal	509	479	479
Grades established by the act of July, 1944 (42 U.S.C. 207):			
Assistant surgeon general grade, $45,148 to $62,878	1	1	1
Director grade $22,241 to $39,193	3	3	3
Senior grade, $22,241 to $39,193	1	2	2
Subtotal	5	6	6
Grade established under 5 U.S.C. 3104	1	1	1
Ungraded	1	1	1
Total permanent positions	529	501	501

DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

Buildings and Facilities

FY 1987 Budget

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NATIONAL INSTITUTES OF HEALTH

Buildings and Facilities

For construction [of,] and acquisition of [sites and] equipment for[,] facilities of or used by the National Institutes of Health [$14,900,000] *$8,000,000*, to remain available until expended. *(Department of Health and Human Services Appropriation Act, 1986.)*

NATIONAL INSTITUTES OF HEALTH

Buildings and Facilities

Amounts Available for Obligation[1/]

	1985	1986	1987
Appropriation	$21,730,000	$14,900,000	$ 8,000,000
Enacted administrative reduction	---	---	---
Sequester order	---	-641,000	---
Proposed rescission	---	---	---
Subtotal, adjusted appropriation	21,730,000	14,259,000	8,000,000
Unobligated balance, start of year	14,024,000	20,080,000	---
Unobligated balance, end of year	-20,080,000	---	---
Total obligations	15,674,000	34,339,000	8,000,000

[1/] Excludes the following amount for reimbursable activities carried out by this account: 1985 -- $58,000.

Buildings and Facilities

Summary of Changes

1986 Estimate, current budget authority	$ 14,259,000
1987 Estimate, budget authority	8,000,000
Net change	-6,259,000

Increases:

A. Program:

1. Animal Facilities Project	$ +3,000,000
2. Repairs and Improvements	+5,000,000
Total, increases	+8,000,000

Decreases:

A. Program:

1. Clinical Center Modernization	$ -7,082,000
2. Rehabilitation of Laboratory Buildings 2, 3, 4, 5, 7, and 8	-2,392,000
3. Repairs and Improvements	-4,785,000
Total, decreases	-14,259,000

Total, net change	-6,259,000

Buildings and Facilities

Budget Authority by Activity
(Dollars in thousands)

	1986 Appropriation	1986 Available after sequestering	1986 Revised	1987
Research facilities...........	$26,144	$ 25,718	$ 25,718	$ 3,000
Service and administrative facilities..................	8,836	8,621	8,621	5,000
Total obligations...........	34,980	34,339	34,339	8,000
Unobligated balance, start of year...............	-20,080	-20,080	-20,080	---
Unobligated balance, end of year.................	---	---	---	---
Total budget authority......	14,900	14,259	14,259	8,000

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Buildings and Facilities

Budget Authority by Object

	1985 Actual	1986 Estimate	1987 Estimate
Transportation of things.............	-2,000	---	---
(Obligations).......................	(-2,000)	---	---
Rent, communications and utilities..	1,000	---	---
(Obligations).......................	(1,000)	---	---
Printing and reproduction...........	4,000	5,000	5,000
(Obligations).......................	(4,000)	(5,000)	(5,000)
Other services......................	20,262,000	14,104,000	7,845,000
(Obligations).......................	(14,206,000)	(34,184,000)	(7,845,000)
Equipment...........................	1,516,000	50,000	50,000
(Obligations).......................	(1,516,000)	(50,000)	(50,000)
Lands and structures................	-51,000	100,000	100,000
(Obligations).......................	(-51,000)	(100,000)	(100,000)
Total budget authority by object....	21,730,000	14,259,000	8,000,00
(Total obligations by object).......	(15,674,000)	(34,339,000)	(8,000,000)

Buildings and Facilities

Appropriations History

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation[1]
1978	65,650,000	65,650,000	65,650,000	65,650,000
1979	30,950,000	67,950,000	67,950,000	30,950,000
1980	3,250,000	3,250,000	3,250,000	3,250,000
1981	11,750,000	11,750,000	11,750,000	11,750,000
1982	10,310,000	10,310,000	10,310,000	9,898,000
1983	17,500,000	17,500,000	17,500,000	17,500,000
1984	19,900,000	24,980,000	25,100,000	25,040,000
1985	11,100,000	21,730,000	21,700,000	21,730,000
1986	14,900,000	14,900,000	14,900,000	14,900,000
1986 Sequester	-641,000			
1987	8,000,000			

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[1] Reflects enacted supplementals, rescissions, and reappropriations.

Buildings and Facilities

Justification

	1986 Appropriation	1986 Available after sequestering	1986 Revised	1987
Research facilities.............	$ 9,900,000	$ 9,474,000	$ 9,474,000	$ 3,000,000
Service and administrative facilities......................	5,000,000	4,785,000	4,785,000	5,000,000
Total......................	14,900,000	14,259,000	14,259,000	8,000,000

General Statement

This appropriation provides for the design, construction, improvements and major repair of clinical and laboratory buildings and supporting facilities essential to the mission of the National Institutes of Health. Except for the continuing programs of major repairs and improvements, funds are provided for non-recurring direct construction projects. All funds are available until expended.

Buildings and facilities funded under this appropriation include those required for both research programs and support services at the main NIH Reservation, Bethesda, Maryland, totalling 60 buildings and more than six million gross square feet of space. Additional facilities are the NIH Animal Center, Poolesville, Maryland; the NIEHS facility in Research Triangle Park, North Carolina; the Rocky Mountain Laboratory, Hamilton, Montana; the Gerontology Research Facility, Baltimore, Maryland; the Primate Facility, Perrine, Florida; and other NIH field stations.

Overall Budget Policy

The 1987 budget request for Buildings and Facilities is $8,000,000, $6,900,000 less than the 1986 estimate. It provides for the renovation of existing animal facilities and construction of new facilities to meet accreditation standards by October 1987 and the continuation of the programs for repairs and improvements to facilities.

Buildings and Facilities

Program Accomplishments

Other than the addition to NIH's real property holdings in 1983 of the Convent of the Sisters of the Visitation of Washington, the size of the facility at Bethesda has remained unchanged during the past several years. New construction projects that are ongoing, having been initiated and approved in prior years, are: the renovation of six of the campus' older laboratory buildings, a project begun in 1981; and modernization of the NIH Clinical Center, begun in 1979.

The continuing program of repairs and improvements includes activities of a routine, short-term nature required as the result of constant use, exposure to the elements, and changes in space utilization. Such activities normally involve the repair and improvement to building structures and systems; repair to roads, sidewalks and parking areas; fire and safety improvements; replacement of elevators and roofs; energy conservation improvements; accommodations for the handicapped; and renovations of space to accommodate new purposes.

Buildings and Facilities

Research Facilities

1987 Authorization: Indefinite.

Budget Authority:

1986 Appropriation	1986 Available after sequestering	1986 Revised estimate	1987	Increase or decrease
$9,900,000	$ 9,474,000	$ 9,474,000	$3,000,000	$-6,474,000

Purpose and Method of Operation

This activity provides for the design and construction of new facilities for the NIH research programs.

Rationale for the Budget Request

The 1987 estimate for Research Facilities is $3,000,000 and provides for the renovation of existing animal facilities and construction of new facilities.

Animal Facilities Project

1987 Budget Request..$3,000,000

With increased public interest in the use and care of animals in research, NIH administration is concerned that its own facilities for housing and utilizing animals meet its own guidelines on animal use and care, as well as others that will be promulgated as the result of recently enacted legislation. Approximately 80 percent of NIH intramural animal holding space meets the standards of the American Association for Accreditation of Laboratory Animal Care, leaving 83,000 square feet of unaccredited space. The NIH has established a goal of insuring that all animal facilities on the NIH campus meet the AAALAC standards by October 1987. An Oversight Committee on AAALAC accreditation has considered plans for bringing facilities up to the required standards through policy development, management improvements, such as the contracting of some animal care activities, and facility renovation and construction.

The Committee has identified two phases of activities for the NIH intramural animal facilities. The first phase, of two-year duration, would involve the consolidation of existing animal facilities within individual buildings, renovation of existing space, and new construction; the second phase, of 5 to 10 years, would require the greater consolidation of scattered animal holding activities and construction of new facilities. The plan and scheduling is complicated by the ongoing renovation of laboratory buildings and the need to minimize disruption to that project's progress and to the laboratories affected.

The 1987 request will permit progress under the first phase of this plan by providing funds for the consolidation of some of the existing animal facilities, renovation, and construction.

Buildings and Facilities

Service and Administrative Facilities

1987 Authorization: Indefinite.

Budget Authority:

1986 Appropriation	1986 Available after sequestering	1986 Revised estimate	1987	Increase or decrease
$5,000,000	$4,785,000	$4,785,000	$5,000,000	$+215,000

Purpose and Method of Operation

This activity includes the continuing program of repairs and improvements to existing buildings and facilities, and to those under design or construction, that house research and administrative activities.

Rationale for the Budget Request

The 1987 estimate for Service and Administrative Facilities is $5,000,000. It provides for continuation of the program of repairs and improvements to existing facilities.

Repairs and Improvements

1987 Budget Request..$5,000,000

The Repairs and Improvements program applies to the physical plants at Bethesda, Poolesville, and Baltimore, Maryland; Research Triangle Park, North Carolina; Hamilton, Montana; Perrine, Florida; and other field stations for which NIH has the property holding responsibility. Program-related repairs and improvements are required to accommodate changes in the direction of research efforts.

Some of these costs are for items such as roofs, roads, and underground utilities that require maintenance in order to retain sound operating conditions. Others are largely non-recurring purchases of equipment or parts that require unpredictable replacement or repair. Activities supported with these funds are relatively small and unanticipated to the extent that lead time is not sufficient to request funds during the regular budget cycle.

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